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## GASTRIC NEURECTOMY FOR GASTRIC AND DUODENAL ULCERATION\*

AN ANATOMIC AND CLINICAL STUDY

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DRAGSTEDT's<sup>1</sup> interesting studies on the effect of resection of the vagus nerves in more than 100 cases of peptic ulcer and similar promising studies by Grimson, Moore and their associates<sup>2, 3</sup> have led us to attempt to study the problem from the anatomic, clinical and experimental standpoint. We began our work by an anatomic study of the distribution of the vagus nerves above and below the diaphragm in order to determine their relative position, number and size and whether the thoracic or abdominal approach to them along the lower part of the esophagus and the upper part of the stomach was best. In dissection in more than 100 cases at necropsy (56 men, 44 women and 11 children) we found, as Miller<sup>4</sup> previously found, a marked variation in the anatomic distribution of the vagus nerves, which in the present study of their relation to the lower part of the stomach and esophagus we shall term "gastric nerves."

Because of the bizarre results following resection of the vagus nerves in experimental animals, we have reviewed the literature on the subject and also the reports of the results of the operation in the treatment of peptic ulcer of human beings to November 1, 1946. Resections of the vagus or

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gastric nerves have been done at the Mayo Clinic in the treatment of peptic ulcer in 66 cases. In this paper we are reporting on the immediate results of the operation performed by one of us (W W) on 33 patients (Tables I, II and III), and are commenting on the indication for the operation. Brief mention also will be made of 33 cases in which other surgeons at the clinic performed the operations. Some of these are listed in Table IV.

Denervation of the stomach is not a new concept in the treatment of peptic ulcer, and an extensive and confusing literature has appeared since Brodie's<sup>5</sup>

TABLE I  
GASTRIC NEURECTOMY (VAGOTOMY) AUTHORS' CASES

Case	Lesion	Total and Free Acids and Gastric Contents		Minimal Blood Sugar Mg per 100 cc	Curve of Insulin Test	Roentgenologic Findings	Comment and Results
		Before Operation	After Operation				
1	Gastro-jejunal ulcer	28/12 45 cc	40/0 40 cc	20	Flat		Good relief
2	Gastro-jejunal ulcer	32/16 60 cc	12/0 75 cc (night)	33	Flat	Moderate delay in emptying	Excellent relief
3	Gastric ulcer		26/0 60 cc (night)	53	Flat	Atonic stomach, considerable secretion	Good relief early but persistence of retained secretions
4	Gastric ulcer		20/0 500 cc (night)	22	Downward	Normal motility	Good relief
5	Bleeding duodenal ulcer		10/0				Retention of 900 to 2 300 cc 4 to 9 postoperative days Dramatic relief
6	Duodenal ulcer	64/54 75 cc	6/0 141 cc (night)	23	Downward		
7	Duodenal ulcer	46/24 150 cc	40/28 100 cc	7 (incorrect)	Upward		Good relief
8	Duodenal ulcer	56/46 115 cc	14/0 10 cc	76	Upward	Normal	Good relief
9	Duodenal ulcer	60/40	20/0 50 cc			Duodenal ulcer with no crater, normal motility	Good relief
10	Duodenal ulcer	64/52 130 cc	34/20 450 cc (night)	28	Downward	Considerable secretion in stomach	Good relief

first reports, in 1814. With the exception of those in the most recent reports, results have been diversified and often conflicting. The extent of the operation has varied in the hands of different workers and the fact must not be overlooked that many workers have employed it in the experimental production of peptic ulcer.<sup>6</sup> That there is no agreement on even the morphology of the structures of these nerves, let alone their function, is reflected in recent reports in which one author<sup>7</sup> concluded that the vagus nerve is composed of nothing but sympathetic fibers, whereas two other investigators denied the presence of any sympathetic fibers in the nerve.<sup>8</sup>

# GASTRIC NEURECTOMY FOR ULCER

Our anatomic observations were focused particularly on the nerve structures from the pulmonary plexuses to the stomach. The vagi invariably break up into a number of branches immediately below the pulmonary plexus, cross-communicate on the esophagus where they are joined by sympathetic fibers to form the so-called esophageal plexus. In 92 of the specimens from adults studied at necropsy a rather regular pattern was followed in forming

TABLE II  
GASTRIC NEURECTOMY PLUS SIMULTANEOUS GASTRO-ENTEROSTOMY

Case	Type of Gastro-enterostomy	Lesion	Total and Free Acids and Gastric Contents		Minimal Blood Sugar, Mg per 100 cc	Curve of Insulin Test	Roentgenologic Finding	Comment and Results
			Before Operation	After Operation				
11	Posterior	Duodenal ulcer, with obstruction	70/56 375 cc	26/16 30 cc	32	Downward		Excellent relief
2	Posterior	Perforating duodenal ulcer	98/88 150 cc					Good relief
3	Posterior	Hemorrhagic duodenal ulcer with obstruction	78/66 275 cc	10/0 370 cc			Normal	Good relief
4	Posterior	Perforating duodenal ulcer	70/54					Good relief
5	Posterior	Perforating duodenal ulcer with obstruction	80/68	16/0 100 cc			Normal	Good relief
6	Posterior	Perforating duodenal ulcer, with obstruction	80/60	40/0 60 cc (night)	32	Downward	Gastrosplasm	Good relief
7	Posterior	Duodenal ulcer	46/30 17 cc	16/0 600 cc (night)	50	Flat	Normal	Good relief
8	Posterior	Duodenal ulcer, with obstruction	78/54 200 cc	8/0 13 cc	22	Flat	Dilatation with retained secretions	Slight fullness with food, good relief of symptoms
9	Posterior	Penetrating bleeding duodenal ulcer with obstruction		34/22			Rapid emptying of stomach, delay in small bowel	Ileus, exploration 800 cc retention
10	Posterior	Duodenal ulcer with obstruction	66/54 100 cc	22/16 100 cc			Deformed duodenum Gastro-enterostomy free but high	Retention of 2,000 cc 4 to 14 post-operative days, recurrence, pain and vomiting
1	Posterior	Duodenal ulcer	32/18 500 cc	14/0 300 cc (night)	45	Flat	Edema at anastomosis	Slight fullness with meals Good relief
2	Anterior, entero-anastomosis later	Duodenal ulcer with obstruction	60/50 175 cc	46/26			Obstruction for 14 days	Obstruction for 26 days, good relief
3	Anterior	Duodenal ulcer with obstruction	60/40	64/54 200 cc			Considerable retention	Retention of 900 cc on 4 postoperative days, poor relief



TABLE III

## GASTRIC NEURECTOMY PLUS SIMULTANEOUS GASTRIC OPERATIONS

Case	Lesion	Total and Free Acids and Gastric Contents		Minimal Blood Sugar Mg per 100 cc	Curve of Insulin Test	Roentgenologic Findings	Comment and Results
		Before Opera- tion	After Opera- tion				
Gastro enteric Anastomosis Disconnected, Ulcer Excised							
24	Gastrojejunal ulcer		20/6 125 cc (night)	30	Flat	Slight deformity duodenal cap, jejunitis in prox- imal jejunum	Excellent relief
25	Gastrojejunal ulcer	58/42 200 cc	10/0 80 cc (night)	43	Downward		Excellent relief
Gastro enteric Anastomosis Disconnected, Ulcer Excised, Heineke Mikulicz Pyloroplasty							
26	Malfunction- ing stoma with obstruction	72/60 55 cc	84/50 150 cc (night)	30	Downward	Gastric pyloric spasm	Good relief
Gastro enteric Anastomosis Disconnected, Ulcer Excised, Finney Pyloroplasty Operation							
27	Gastrojejunal ulcer	54/40 260 cc	60/36 800 cc (night)	20	Downward	Duodenum de- formed by previous ulcer, stomach slightly atonic	Early retention, grad- ual decrease in 4 to 6 days Good relief
Gastro enteric Anastomosis Disconnected, Anterior Polya Resection							
28	Gastrojejunal ulcer	24/10 104 cc	6/0 50 cc			Free anastomosis, bowel negative	Good relief
Duodenal Ulcer Excised, Gastroduodenostomy							
29	Duodenal ulcer	66/48 200 cc	22/0 325 cc (night)	36	Flat		Good relief
Biopsy of Ulcer and Caутery							
30	Gastric ulcer	12/0	22/0 50 cc (night)				Good relief
Transthoracic Exploratory Gastrotomy, Biopsy of Gastric Ulcer, Gastric Closure							
31	Gastric ulcer and duodenal ulcer	64/52	22/0 800 cc (night) 11-11-46 40/26 250 cc	45	Downward	Recurrence of ulcers but essen- tially normal emptying of stomach	Moderate early reten- tion, poor result
Gastric Ulcer Explored							
32	Gastric ulcer Healed duo- denal ulcer	50/34 180 cc	28/0 200 cc	45	Upward then downward	Normal	Good relief
Exploratory Gastrotomy Only							
33	Gastritis	54/42 380 cc	8/0 40 cc	76	Upward	Normal	Good relief

GASTRIC NEURECTOMY FOR ULCER

discrete nerve trunks below the esophageal plexus In 64 of these the nerve trunks formed between the esophageal hiatus and 6 cm above the diaphragm, in 21, at the distance of 6 cm above the diaphragm, and in seven at the esophageal hiatus In eight of the dissections, it was impossible to isolate two distinct trunks at any point In these eight cases the nerves were numerous and communicating, and their distribution did not follow a uniform pattern

The position of the right and left trunks below the esophageal hiatus was noted in 92 cases, and was found to be remarkably constant The right gastric

TABLE IV  
GASTRIC NEURECTOMY (VAGOTOMY) SIGNIFICANT CASES OF OTHER SURGEONS

Case	Transthoracic Approach for	Free and Total Acids and Gastric Contents		Minimal Blood Sugar Mg per 100 cc	Curve of Insulin Test	Roentgenologic Findings	Comment and Results
		Before Operation	After Operation				
34	Gastrojejunal ulcer	54/46 185 cc	20/0 210 cc				Excellent relief
35	Gastrojejunal ulcer	62/52 100 cc	14/0 90 cc	37	Flat	No ulcer Temporary delay in jejunum	Good relief
36	Gastrojejunal ulcer	36/26 105 cc	18/0 80 cc			Free anastomosis No gastrojejunal ulcer	Good relief
37	Gastrojejunal ulcer	1944 112/100 150 cc 1945 40/20 100 cc	12/0 50 cc				No pain, slight tendency to diarrhea
38	Duodenal ulcer	60/46 130 cc	50/28 200 cc	38	Downward		Good relief
39	Duodenal ulcer	78/68 100 cc	5-31-36 26/12 320 cc 6-1-46 62/50 150 cc	-			Early retention, good relief, considerable eructation
40	Duodenal ulcer (abdominal approach)	74/56 150 cc	40/20 40 cc				Early retention Intermittent vomiting and diarrhea

nerve, the larger in 54 cases, coursed posteriorly and to the left and then broke up into its branches about 3 to 5 cm from the hiatus The largest branch of the right nerve invariably traveled along the left gastric artery to the celiac plexus The left nerve followed a much shorter course in the abdomen As it emerged onto the anterior surface of the stomach, it divided into numerous small branches which were lost in the serosa and musculature of the stomach A branch from both the right and left nerves was invariably found entering the leaves of the gastrohepatic omentum

From the anatomic standpoint, therefore, it would appear that in a trans-abdominal approach to the gastric nerves the nerves could be located suc-

cessfully in approximately 92 per cent of the cases, and possibly many of the branches in the remaining 8 per cent. In the 33 cases in which one of us (W W) resected the vagus nerves (gastric neurectomy) through the transabdominal route, in every case but one it has been possible by exercising care, to find all the gastric nerves, as proved by the Hollander<sup>9</sup> insulin test.

From the experimental standpoint, I should like to consider several important points. As stated earlier in the paper, an extensive review of the literature reveals that in many instances the early and late effects of gastric denervation in experimental animals have been confused, the results in man have been compared indiscriminately with those in lower animals, and the extent of the operation experimentally, and clinically, has varied in the hands of different workers.

Seventeen years ago, working in the Division of Experimental Surgery of the Mayo Foundation, Hartzell,<sup>10</sup> and Vanzant<sup>11</sup> studied the effects of intrathoracic and abdominal section of the vagus nerves of dogs. Hartzell<sup>10</sup> first studied eight animals, on six, intrathoracic vagotomy had been performed and, on two, abdominal vagotomy. The immediate findings revealed total abolition of psychic secretion (cephalic phase), marked and constant reduction in the quantity of free hydrochloric acid and of the total acids and an increase in the hydrogen ion concentration of the gastric secretion. Vanzant<sup>12</sup> studied some of the same group of dogs and an additional group two and one-half years later, and found that in all of the dogs of the original group that she studied the amount of total and free acid had increased five to six months after operation and that free acid was present in all but one of the original group studied two to three years after operation. Eventually, in four of the dogs, curves of free and total acid approach normal. Effects of vagotomy on motility of the stomach were inconstant. Early studies recently reported by Vanzant<sup>11</sup> disclosed that in four dogs delayed emptying of the stomach occurred, two dogs had hypermotility with a tendency to diarrhea and emesis, and three dogs had no change in emptying time. Later results<sup>12</sup> showed the motility of seven of ten dogs to be essentially normal. The general health of six dogs was not impaired except for excessive salivation which gradually lessened. Two dogs vomited frequently following the operation. Three dogs had increased appetites in spite of which they lost weight. Of these, two also had a tendency toward diarrhea.

Vanzant's<sup>11</sup> comments on these studies were that the psychic phase of secretion seemed to be abolished and the ability of the secretory mechanism to respond to stimuli was decreased. Excessive secretion of mucus was one of the most striking and typical results of vagotomy. She mentioned several possible explanations for the gradual increase of gastric secretion as follows: 1. Regeneration of the severed nerves was considered, but this had not occurred in two dogs on which second operations were performed nor in one dog, as determined at postmortem examination. She assumed, therefore, that regeneration was not an important factor. 2. The possibility that resumption of secretory function was due to stimulation of sympathetic fibers of splanchnic nerves was considered. In three dogs, however, the splanchnic nerves had

been cut at the time of gastric neurectomy, still, secretion was resumed. She concluded, therefore, that the parasympathetic fibers were not essential in the restoration of gastric secretion. 3 Spontaneous restoration of tone by the autonomous motor and secretory mechanism was the only mechanism she was unable to rule out by her experiments, and she concluded that this mechanism might be responsible for the restoration of gastric acidity. The conclusion which all should draw from this experimental study is that time must elapse before the ultimate results of gastric neurectomy on the secretory and motor activities of the stomach can be determined.

#### CLINICAL APPLICATION

*The Approach and Associated Operations*—The clinical application of these anatomic studies has led one of us (W W) to believe that the best approach to the gastric nerves is by an incision in the upper part of the abdomen. The advantage of this approach is that, in addition to permitting abdominal exploration to exclude disease of other organs, it permits examination of the ulcer, its removal if it is a gastric ulcer and is suspected of being malignant, or some type of drainage operation of the stomach if the ulcer is duodenal and obstructive, or if it would appear that obstruction might follow resection of the gastric nerves.

Patients upon whom gastric neurectomy is carried out usually have complicated chronic ulcers which have not responded to many attempts at non-surgical (medical) treatment. If a gastrojejunal ulcer is present which has followed gastro-enterostomy, obstruction not infrequently is present also, as a result of repeated ulceration at the stoma and with the obstruction the previously existing duodenal ulcer frequently is reactivated. In such cases, in addition to gastric neurectomy removal of the gastrojejunal ulcer and the gastro-enterostomy seems necessary, and if obstruction of the duodenum had resulted from reactivation of the duodenal ulcer or from its healing following the gastro-enterostomy, a pyloroplasty seems indicated. In one case in which a recurring ulcer followed a gastric resection, performed elsewhere, perforation of the anastomotic ulcer into the colon was impending. In this case extensive gastric resection seemed indicated together with removal of the anastomotic ulcer, even though gastric neurectomy also was done. It is easy to understand, therefore, why gastric neurectomy has been performed without some other surgical procedure on the stomach of the type mentioned in only ten of the 33 cases in which the operation was performed by one of us (W W).

*Results*—Since the various surgical procedures on the stomach just mentioned when used without gastric neurectomy in the treatment of patients with ulcers have been followed by relief of pain, decrease of night secretion, reduction of gastric acidity and relief of gastrospasm, the difficulties of determining the effect of associated gastric neurectomy in such cases is evident. This has been true in a study of the 66 patients who have undergone gastric neurectomy during the past year at the Mayo Clinic. Gastric neurectomy has been performed in 23 cases without any other surgical procedure on the stomach (Table V). In this paper it has seemed best to us to

report mainly the results in 33 cases in which one of us (W W) performed the operation (Table VI) However, occasionally reference will be made to other cases

The immediate results in ten of our cases in which resection of gastric nerves was done without other surgical procedures on the stomach have been satisfactory thus far (Table I) Relief of pain, reduction in gastric secretion, reduction of gastric acidity, with early achlorhydria in most cases, and relief of gastrosplasm have occurred However, some interesting complications have occurred in these as well as in the group of 23 in which associated gastric operations were done (Tables II and III) One patient, who had undergone gastric neurectomy only, had sufficient gastric atony and sufficient increase of gastric secretion to require intermittent gastric drainage from the 4th to 9th

TABLE V  
GASTRIC NEURECTOMY  
CASES AT MAYO CLINIC TO NOVEMBER 1 1946

Type of Operation	Total Cases	Duodenal Ulcer	Gastro-juncal Ulcer	Gastric Ulcer	Gastritis
Gastric neurectomy only	23	11	10	2	0
Gastric neurectomy with gastro enterostomy	29	29	0	0	0
Gastric neurectomy with excision of ulcer	14	4*	7†	3*	1
Total	66	44*	17†	5*	1

\* Both duodenal and gastric ulcer in one case

† Gastrojejunal fistulae in two cases

day after operation (Table I) In three additional cases moderate retention of gastric secretion was revealed on roentgenoscopic examination, in one, several weeks after operation (Case 3, Table I) In one of 13 additional cases, in which our surgical colleagues at the Mayo Clinic performed gastric neurectomy only, gastric acidity and symptoms of ulcer returned in six weeks in spite of achlorhydria immediately after operation (Table IV) Two patients in that same group have had intermittent diarrhea

Postoperative disturbances in gastric motility have been troublesome in seven of our 23 cases in which other gastric operations were associated with gastric neurectomy (Tables II and III) Characteristic of three of these, were intermittent paroxysmal abdominal distention relieved by injections of neostigmine In one of the three cases (Case 19), in which gastro-enterostomy and gastric neurectomy were done, abdominal distention appeared on the 5th postoperative day and increased during the next two days Roentgenologic studies of the abdomen revealed what seemed to be an obstruction of the small intestine Exploration revealed ileus, the small intestine was filled with fluid and air or gas, and approximately 800 cc of sterile straw-colored fluid was found in the peritoneal cavity Continuous gastric suction by means of an indwelling nasal suction tube relieved the distention and normal intestinal motility returned

## GASTRIC NEURECTOMY FOR ULCER

In four additional cases gastric retention was troublesome for a few days and in all but one of these it subsided within a week. In one case (Case 22) jejunojejunostomy was necessary on the 26th postoperative day to relieve persisting gastric retention. In one case (Case 31), that of a Jew, 67 years of age, a recurrence of a gastric ulcer had taken place, with severe clinical symptoms in spite of a positive insulin test, showing a complete severance of all the gastric (vagus) nerves. An early achlorhydria had been followed by a return of gastric acids.

TABLE VI  
GASTRIC NEURECTOMY  
AUTHORS' CASES TO NOVEMBER 1, 1946

Type of Operation	Total Cases	Duodenal Ulcer	Gastro jejunal Ulcer	Gastric Ulcer	Gastritis
Gastric neurectomy only	10	6	2	2	0
Gastric neurectomy with gastro enterostomy	13	13	0	0	0
Gastric neurectomy, with excision of ulcer	10	2*	5	3*	1
Total	33	21*	7	5*	1

\* Both duodenal and gastric ulcers in one case

TABLE VII  
COMPLICATIONS FOLLOWING GASTRIC NEURECTOMY IN FIRST 66 CASES (ALL SURGEONS)

Type of operation	Total cases	Retention		Results	
		Early clinical	Roentgenologic	Cases	Type
Gastric neurectomy only	23	6	6	1	Early pleural effusion, epigastric distress
				1	Recurrent abdominal pain
				1	Tendency to slight diarrhea
				1	Early retention followed by intermittent emesis and diarrhea
				1	Considerable belching
				1	Died fourth postoperative day, probably pulmonary embolus
				1	Died fourteenth postoperative day from perforated duodenal ulcer and subdiaphragmatic abscess
Gastric neurectomy with gastro-enterostomy	29	8	3		
Gastric neurectomy with excision of ulcer or other operation on stomach	14	1	3	1	Died of unknown cause three months after operation
				1	Recurrent night pain

In one of the cases in which gastric neurectomy and gastro-enterostomy were performed by our colleagues, the duodenal ulcer perforated (Table VII). A subdiaphragmatic abscess developed, and the patient died on the 14th postoperative day. In another case in which gastric neurectomy, cholecystectomy and appendicectomy were performed, the patient died following a convulsion on the 4th postoperative day. Postmortem examination was not performed.

Another death from unknown causes\* occurred at the patient's home three months after gastric neurectomy for gastrojejunal fistula in which the fistula into the colon was closed at the time of operation

The gastric acid of one additional patient who had an early relative achlorhydria returned to preoperative level one month after operation and symptoms of ulcer returned. An insulin test was not done in this case.

Gastric acidity and gastric secretion in the cases in which gastric neurectomy alone was performed on our service and some of the other services and in those in which gastric neurectomy was associated with other gastric operations are shown in Tables I to IV and VIII. In many cases in each

TABLE VIII  
FREE GASTRIC ACIDITY IN RELATION TO TYPE OF GASTRIC OPERATION (AUTHORS' CASES)

Type of Operation	Total Cases	Acidity Before Operation		Acidity After Operation	
		Determinations made Cases	Mean Value Units	Determinations made Cases	Mean Value Units
Gastric neurectomy only	10	7	30.0	10	2.8
Gastric neurectomy and gastro-enterostomy	13	12	53.2	11	12.2
Gastric neurectomy and excision					
Gastrojejunal ulcer	5	4	38.0	5	18.8
Gastric ulcer	3	3	20.0	3	0
Duodenal ulcer	1	1	48.0	1	0
Gastritis	1	1	42.0	1	0
All cases	10	9	33.6	10	9.4
Grand total	33	28	41.1	31	8.3

group, postoperative studies of gastric motility and roentgenoscopic and roentgenographic examinations were made on approximately the 16th to the 20th day after operation. The temporary changes in gastro-intestinal motility pattern have been described.

*Insulin Test*—It is, of course, important in evaluating results of gastric neurectomy to determine whether all of the gastric (vagus) nerves have been divided. Unfortunately, the insulin test, described by Hollander,<sup>9</sup> involves some risk and must be done only under the constant supervision of a physician who has available a solution of glucose for immediate administration if symptoms and signs of impending hypoglycemic convulsions become manifest. The test itself consists of injection of 10 to 30 units of insulin in order to reduce the patient's blood sugar to 30 mg per 100 cc. If branches of the gastric nerves are intact, the gastric secretion increases 40 to 50 minutes after injection of the insulin. In 20 of the 66 cases in which gastric neurectomy was performed at the clinic, the Hollander insulin test has been carried out. Results are shown in Tables I to IV. In all but one of our 33 cases (W. W.) no elevation in gastric acidity occurred (Tables I to IV).

\* Death due to heart disease reported by home physician

We are indebted to Drs Fitzgibbons, Watts, McVicker, Brownson, Lowe and Lyman for assistance in reviewing and abstracting the records, and tabulating the results

Case 31—A Jew, age 67, gave a history of having had peptic ulcer for 36 years. Posterior gastro-enterostomy was performed in July, 1927, for a small duodenal ulcer. Shortly after operation, intermittent attacks of abdominal pain of ulcer type began. A gastrojejunal ulcer was demonstrated on roentgenologic examination on several occasions, and medical treatment was given without relief.

Symptoms of ulcer became more severe in April, 1946. Roentgenologic examination revealed a large perforating gastric ulcer on the lesser curvature of the stomach just below the esophagus and a duodenal ulcer. In June, 1946, the gastro-enteric anastomosis was disconnected and the gastrojejunal ulcer was excised. The scar of a healed duodenal ulcer, 4 mm in diameter, was found on the anterior wall of the duodenum but there was no duodenal deformity. The posterior duodenal wall was soft. Transabdominal

TABLE IX  
RESULT OF INSULIN TEST IN CASE 31

	Fasting	Time After Injection of Insulin			
		15 Mins	30 Mins	45 Mins	60 Mins
Blood sugar, mg per 100 cc	103	89	68	48	45
Total acid units	26	12	12	10	10
Free acid units	10	0	0	0	0
Amount of secretion cc.	30	10	15	35	40

gastric neurectomy seemed to be contraindicated at this time because of the location of the perforating ulcer. In order to perform this operation the ulcer would have had to be separated from the pancreas. The high location of the ulcer would have made its removal and accurate closure of the opening in the stomach difficult and hazardous. It was decided that resection of the stomach to remove the ulcer would have necessitated removal of most of the stomach. Since the patient's general condition did not permit a resection of this magnitude, medical regimen seemed indicated. A six-weeks' trial of medical treatment did not give relief of the pain. The gastric ulcer did not decrease in size and a duodenal ulcer, with a crater, was found on roentgenologic examination. Trans-thoracic resection of the gastric nerves was performed on July 9, 1946. One major and one minor anterior nerve and one major and one minor posterior nerve were resected. Incision was made through the diaphragm. Part of the gastric ulcer was excised for microscopic examination and proved to be inflammatory. The opening in the stomach was closed. Subsequent to operation, the patient complained of pain along the thoracic incision, and within two to three weeks pain of ulcer returned. September 18, 1946, a Hollander insulin test was performed with the results shown in Table IX.

The patient has continued to have symptoms of ulcer, regardless of the strict medical regimen carried out in the hospital. Roentgenologic examination on November 13, 1946, showed the gastric ulcer to be practically the same size as prior to operation. Gastric analysis on November 11 revealed 26 units of free hydrochloric acid, with a combined acidity of 40 units. There was 250 cc of gastric secretion. Resection of the stomach was done on January 13, 1947. The ulcer was 2.5 cm in diameter and benign.

COMMENT Dragstedt's first gastric neurectomy in treatment of gastric disease was performed three and one-half years ago, and that of Moore and



Chapman more than two years ago. Since their first operations these surgeons have treated other patients in this manner, most of whom have been benefited. Yet, because of experimental evidence that any change may be only temporary and because long experience with peptic ulcer makes us reserve judgment of any operation until a large series of cases has been collected and a period of many years has elapsed, gastric neurectomy at present, at the Mayo Clinic, is being performed only in selected cases of peptic ulcer. We think the final report on this operation is not due for some years and that all reports now, and for some years to come, should be considered interim reports. In the meantime, the procedure can be used in the following group of cases:

First, in cases of recurring ulcer after an adequate gastric resection, it seems justifiable to undertake the comparatively simple operation of gastric neurectomy on the chance that the ulcer will heal and symptoms will be relieved.

Second, the operation may be used in certain cases of gastric ulcer in which excision of the ulcerating lesion is necessary to exclude the possibility that it is malignant. Microscopic examination is made immediately to eliminate the possibility that the ulcer is an ulcerating carcinoma. Then the gastric neurectomy is performed.

Third, the operation may be undertaken in certain cases of obstructing duodenal ulcers associated with high gastric acidity. Simultaneous gastro-enterostomy is performed to relieve the duodenal obstruction. It will be interesting to determine whether the incidence of recurring ulcers will be less than in cases in which gastro-enterostomy without gastric neurectomy is performed.

A fourth group consists of cases of chronic, nonobstructing duodenal ulcer, in which the cephalic phase of the hyperacidity seems to overshadow other factors and no response has been obtained from repeated courses of medical treatment. In these cases we believe gastric neurectomy may be justified. Many of these patients are young and have high values of gastric acidity and active duodenal ulcers which respond unsatisfactorily to medical treatment. The behavior pattern in these cases suggests a prolonged and excessive nervous phase of gastric secretion.

#### SUMMARY AND COMMENT

A study of the anatomy of the gastric nerves has demonstrated that in 92 per cent of the cases the nerves pass through the diaphragm as two distinct trunks and are readily accessible for resection.

The abdominal approach to the gastric nerves allows exploration of the abdominal contents and especially the ulcer, removing it if it is a gastric ulcer and is suspected of being malignant, and performing a drainage operation of the stomach if the duodenal ulcer is obstructive or likely to become obstructive from gastric atony.

It is important to remember in our series of 33 cases that the disturbances of gastro-intestinal motility were for the most part, temporary. Although

spasm of the pylorus with dilatation of the stomach and hypermotility of the intestine has persisted for several weeks in one patient operated upon for gastric ulcer. In one case gastric ulceration definitely recurred. In the entire series of 66 cases, perforation of a duodenal ulcer and a subdiaphragmatic abscess caused the death of the patient 14 days after gastric neurectomy and gastro-enterostomy, and two other deaths occurred, one from a suspected cerebral embolism on the 4th postoperative day and the other at home from a heart lesion. This patient had had a gastrojejunal fistula closed and gastric neurectomy three months previously. In the other cases the immediate results, as evidenced by reduction in gastric acidity, gastric secretion, relief of gastro-spasm and relief of pain, were good but not striking. If the good results will persist, the operation offers an easy and a comparatively safe method of treating certain cases of peptic ulcer, especially cases of recurrent ulcers. It will have a limited application in cases of obstructing duodenal ulcer and in certain cases of gastric ulcer. In the former, it can be used in a few cases in association with gastro-enterostomy. In cases of gastric ulcer excision of the ulcer should be done to exclude malignancy. When excision of the ulcer and gastric neurectomy have been done simultaneously, disturbances in gastric motility, with retention and higher secretion, have been troublesome. In any case, however, sufficient time must be allowed to pass to determine whether the good results are temporary as they seem to be in experimental animals and whether untoward results may develop.

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DISCUSSION—DR ARTHUR W. ALLYN, Boston, Mass. This presentation to which you have just listened is very interesting to me. Doctor Walters approaches the problem in a different manner from what we have done at Massachusetts General Hospital. When I read the title of his paper I was considerably perturbed that he had included gastric ulceration in his subject. It has been a great consolation to me that he reports one recurrence in five instances of gastric neurectomy for gastric ulcer. I feel this may help us tremendously in preventing the stampede in the direction of applying this approach to cases that should be subjected to more radical types of surgery. Gastric ulcers are admittedly satisfactory from a surgical standpoint. Furthermore, the mortality rate in gastric resection for gastric ulcer is lower than for any other lesion of the stomach.

It is very difficult to get the medical profession to accept the fact that a gastric ulcer that does not respond completely to conservative treatment may be malignant. We reported before this Association a few years ago our analysis of a group of gastric ulcers diagnosed as benign, and in that series 14 per cent proved to be carcinoma. If we are to improve our results in this terrible disease, that takes such a high toll of life each year, we must insist on a radical attitude in gastric ulcer.

We have taken out more of the nerves than is shown in Doctor Walters' beautiful movie, but all our neurectomies have been done transthoracically. We have had excellent results in nonobstructing duodenal ulcer cases. They do get stasis after operation, but we find this is not a serious problem. We have not combined this operation with other procedures such as gastro-enterostomy, because we feel that we must give vagus resection itself a fair trial. The results so far have been spectacular in nonobstructing duodenal ulcers and in anastomatic ulcer. There were two temporary failures in anastomatic ulcer; they had been operated elsewhere, and, supposedly, had had a classic subtotal resection. However, when their anastomatic ulcers failed to respond to vagus resection, abdominal exploration revealed that the antrum of the stomach had been left *in situ* at the time of their original operation. In both cases the anastomatic ulcer healed after removal of the remaining pyloric segment.

Dr F. D. Moore, in our hospital, has carefully evaluated these patients before operation and followed them afterward. He has done most of these procedures in our clinic so far, and has reported the results in detail.

DR R. L. SANDERS, Memphis, Tenn. Before undertaking vagotomy I went to Chicago to observe Doctor Dragstedt's work. If peptic ulcer is neurogenic in origin, as it undoubtedly seems to be, his operation is on solid ground.

After seeing Doctor Dragstedt perform vagotomy transabdominally, I tried the same procedure on cadavers, then opened the chest. I found we had succeeded in dividing all nerve trunks through the abdomen. We have, therefore, employed no other approach in any of our cases, preferring to determine the nature and extent of the disease before deciding upon the type of operation.

The esophagus is easily approached if one first mobilizes the left lobe of the liver by division of its triangular ligament. It is advantageous to leave the tube in the stomach as a guide; one can, thus, easily locate the esophagus. By drawing the esophagus down three inches, the nerve trunks are placed under tension and may be divided between clamps. About two and one-half inches of the nerve may then be resected. Like Doctor Walters, we have found the right nerve the larger of the two in most cases.

We have employed vagotomy for 13 duodenal ulcers and two gastrojejunal ulcers, a total of 15. In seven of the 13 duodenal ulcer cases we have added a gastro-enterostomy because of obstruction. The results in these seven and the two who had a gastrojejunal ulcer have been most satisfactory. The patients who had vagotomy alone have continued to have a mild degree of distention and have had to observe some dietary restrictions. No doubt these after-effects will clear up as the tonus of the stomach improves and the inflammatory reaction about the pylorus subsides. One can never tell, however, whether the tonus will return to normal or how much obstruction will persist. This is, likewise,

true of the acids. If vagotomy keeps the acids from rising again, we have no fear of further trouble from this source. We are inclined to think that the acids will remain low so long as the motility does not become excessive.

Unquestionably, the risk of vagotomy is much less than that of resection. It seems, moreover, that we will be able to give patients better stomach function with less danger of nutritional deficiencies. Doctor Dragstedt is to be congratulated upon his introduction of the procedure. From his own results after a period of approximately four years, it is an outstanding achievement in ulcer treatment from the standpoint of symptomatic relief, as well as of simplicity and safety.

DR R. ARNOLD GRISWOLD, Louisville, Ky. My experience with resection of the vagus nerves has been limited to not quite 30 cases. The results have been very favorable—so much so, that I am afraid there is danger of us all becoming overenthusiastic, and developing the tendency to cut the vagi for every “bellyache.” In all my cases of ulcer, there has been healing of the ulcer and dramatic relief of pain. In only one case has a drainage operation (gastro-enterostomy) been necessary after vagotomy. In five of the other cases pyloric obstruction was recognized prior to vagotomy and a complementary drainage operation performed.

I do not think the approach makes a great deal of difference. Transthoracic approach is easier for me and, I feel, easier on the patient than the transabdominal approach. A good deal depends on whether the surgeon has an anesthetist who is familiar with thoracic surgery.

Of course, in all cases of questionable diagnosis, the approach should be transabdominal. I do not believe the operation should be undertaken on any gastric ulcers. In one of my cases, performed transabdominally, my gross diagnosis was benign gastric ulcer. Later, the patient died of a lymphosarcoma of the stomach. Another case, with which I am familiar, was explored by a competent surgeon, and a frozen section was taken, with the report of benign ulcer. Vagotomy was done and when the permanent sections came through, the diagnosis of carcinoma made resection imperative. Doctor Allen has brought out the number of gastric carcinomas which may be overlooked, even at the operating table, so that until we have better means of making the diagnosis of carcinoma, vagotomy should be reserved for duodenal or gastrojejunal ulcers.

SLIDE I. This slide shows the average 12-hour night secretions before and after vagotomy on 17 patients—a total of 53 tests. Before vagotomy, the average 12-hour volume of gastric secretion was 1,300 cc, with free acidity of 45 degrees. After vagotomy, an average volume of 270 cc with free acidity of one degree was observed.

SLIDE II. This roentgenogram indicates the result of vagotomy following an improperly performed gastro-enterostomy. This patient had a gastrojejunal ulcer resulting from a gastro-enterostomy, performed elsewhere, several years ago. In addition, there was complete pyloric obstruction. As you see, the gastro-enterostomy is far to the left on the great curvature. Following vagotomy, the atonicity of the stomach caused the tremendous dilatation of the antrum, which you see. This was accompanied by marked stasis, fermentation and putrefaction of retained food in the stomach. He has since obtained complete relief following a Finney pyloroplasty. For this reason, whenever a drainage operation is necessary because of pyloric obstruction, it should be either a pyloroplasty or a gastro-enterostomy as near the pylorus as feasible.

DR EDWIN P. LEHMAN, Charlottesville, Va. At the University of Virginia Hospital a single recent experience suggests a use for vagotomy which has not been discussed this morning—namely, vagotomy for the relief of pain associated with gastric or other intra-abdominal cancer. At transthoracic exploration for a supposed chronic perforation of a gastric ulcer, a huge mass was encountered which was thought to be inflammatory. While awaiting the result of a frozen section taken from the edge of an ulcer, vagotomy was done. When the report of cancer was obtained, the diaphragm and chest were

closed, since the lesion was inoperable. The patient had had persistent severe abdominal pain preceding operation. Following operation the pain disappeared completely. The vagotomy was performed by Dr. Edward V. Siegel, Resident Surgeon, under the direction of Dr. William R. Sandusky, of the Visiting Staff.

This experience, also, may have a fundamental bearing on the relief of pain following benign ulcer of the duodenum. In future explorations, in which inoperable gastric cancer is encountered, we intend to carry it out, if possible, as a routine measure, and suggest that others do the same.

DR. FRANK H. LAHEI, Boston, Mass. This is a situation which is now very similar to many we have been through before. We all know them—gastro-enterostomy, total thyroidectomy, bone plates, total colectomy, and any number of other problems. We have to remember, in relation to gastro-enterostomy alone, the enthusiasm with which it was supported, and the arguments over the percentage of complications. We have to remember that it took 20 years to truly assess the position of this operation, which made many of us reverse our position from that taken earlier in our experience.

This is not a condemnation of vagotomy, but is merely to warn against the over-enthusiasm, with which we frequently are likely to promote something in which we are deeply interested. Recall some of the consequences of this overenthusiasm for total thyroidectomy, and how completely without value it was.

Vagotomy is, however, not at all like total thyroidectomy. It really accomplishes something which is very desirable, particularly in patients with duodenal ulcer. It diminishes acidity, it diminishes hypersecretion, and it diminishes motility. Because the operation is still an unseasoned one, but because we have such a large number of patients with ulcers with which to deal, it is necessary for us to take a position on it, which is as follows. We would, if possible, like to limit vagotomy in patients with duodenal ulcers to those patients in whom another operation, such as gastro-enterostomy, will not have to be done. The reason we would like to limit this operation to this type of case, if possible, is that if many of these patients have both vagotomy and gastro-enterostomy it will not be possible to determine to which procedure a good result can be ascribed. In our opinion, this will serve only to confuse the situation. We realize that this will be difficult to attain because of the fact that in so many of the patients with very bad duodenal ulcers in whom surgery is indicated, some degree of pyloric obstruction will be produced when the ulcer heals, and that this will be further augmented by the atony which is associated with a vagotomy. We would like, because of this, to do all cases of this type when possible transthoracically because of the completeness of the removal of the various branches of the vagi at this level.

In performing, now, 97 total gastrectomies, we have become very familiar with the infradiaphragmatic distribution of the vagi, because it is impossible to undertake total gastrectomies without finding the vagi, putting them on the stretch, and severing them.

The thing I do not particularly like about vagotomy, either supradiaphragmatic or infradiaphragmatic, is the number of drainage operations which have to be done with it. This can be particularly undesirable if at a later period it can be demonstrated that there will be a return of high gastric acidity in some of these cases, because we will again be having to deal, as we have in the past, with gastro-enterostomy, with a considerable number of gastrojejunal ulcers and gastrojejunoecolic fistulae.

We would, particularly, not like to undertake this operation upon patients with gastric ulcers. I have personally taken a position with regard to gastric ulcers which is contrary to the one I have maintained in the past, that is, that all gastric ulcers should be removed. I wish to take this position because of the danger of malignant change in some of them, and because of the fact that it is impossible for anyone, except the pathologist, in some of these borderline cases, to tell whether or not malignancy is present in the ulcer. Some of these patients upon whom subtotal gastrectomy for gastric ulcers under these circumstances would be done, would undoubtedly get well on medical

treatment alone, but since, as already stated, pathologists cannot separate the malignant from the benign ulcer, since the five-year nonrecurrence figures in cancer of the stomach are as bad as they are and, since, in addition, the mortality of subtotal gastrectomy for gastric ulcer in inexperienced hands has largely been abolished, I think that neither vagotomy nor medical treatment should be applied in patients with gastric ulcer. I am bound to say, however, that our Gastro-enterologic Department does not entirely agree with me in regard to 100 per cent surgical treatment of these lesions. I feel sure they agree with me, however, that vagotomy should not be applied to patients with gastric ulcer.

It is very nice to have another operation of this type which can be applied to the patient with duodenal ulcer, but it is wrong to assume that this is the complete answer to the problem. Our position regarding it, therefore, is that if we have a patient who has had a subtotal gastrectomy and he, or she, then has a jejunal ulcer, since this is such a complicated operative procedure at this stage and since this stomach will drain well anyway, we will unhesitatingly apply transthoracic vagotomy to this type of patient. We know that some of our patients with subtotal gastrectomy for ulcer do have gastro-jejunal ulcers, probably about 5 per cent. We know, in addition, that some of our patients operated upon for duodenal ulcer who have had high subtotal gastrectomies bled after the subtotal gastrectomy. We have, therefore, combined infradiaphragmatic vagotomies with our subtotal gastrectomies with the hope that this will diminish the number of jejunal ulcers and bleeding after adequate subtotal gastrectomies for duodenal ulcers.

We must keep our minds open on this subject. It is fine that University Clinics can undertake them, but for us, who have to deal with private patients, many of them in the charity group, but who still take the position that they do represent private patients, it is necessary for us to take a middle-of-the-road position, having in mind always the uncertainty at a later date of the results of these vagotomies and the associated gastro-enterostomies which have to be done with them. We are quite willing to limit our experiences with this operation to the above group until it has been employed in a larger number of cases, over a greater number of years.

DR WALTMAN WALTERS, Rochester, Minn (closing). I should like to thank the gentlemen who discussed my paper. I agree with them, heartily, that gastric resection (partial gastrectomy) is the best surgical method of treating chronic gastric ulcer. I am particularly happy to have Doctor Lahey say that he is of the same opinion. For 20 years we have advocated the practice of resection of the stomach in treatment of chronic gastric ulcer and have carried out such practice in approximately 60 per cent of such cases seen at the Mayo Clinic. In contrast, the incidence of surgical treatment of duodenal ulcers has decreased to about 12 per cent of those found in the clinic. When one operates in only 12 per cent of cases he is operating, then, only on patients with complicated duodenal ulcers, such as those that are causing bleeding, perforation, obstruction or impending obstruction. Therefore, since in the latter conditions operation upon the stomach to provide for drainage will be required sometimes, it is much better to provide for such drainage at the time of gastric neurectomy than to perform a secondary operation a few weeks, or months, later.

I do not agree that gastro-enterostomy is an obsolete operation. Some of the best results I have seen in the treatment of duodenal ulcer are in cases in which gastro-enterostomy has been performed, and jejunal ulcers have not developed. In cases in which the type of operation was properly chosen and properly performed we have not seen recurrences in more than 4 per cent. As a matter of fact, Hans Lorenz, of Vienna, who first advocated use of gastric resection routinely in treatment of duodenal ulcer, told me that in his own experience he had never seen recurrences of duodenal ulcer in more than 10 per cent of cases after gastro-enterostomy had been performed in a proper manner. These operations had been performed on central Europeans whose nutritional state from 1918 to 1930 had been rather poor.

I should like to concentrate attention on the terminology we should all adhere to. The term "vagotomy" is not descriptive of the operation in which a section of the vagus nerve is removed. I think a better term would be either "gastric neurectomy" or "vagus nerve resection." Although I think it makes little difference whether the approach is made above or below the diaphragm in isolation of the vagus nerves, I prefer the subdiaphragmatic approach because it permits exploration of the lesion and abdominal contents. In all but one of my cases the approach has been from below the diaphragm. The findings in anatomic dissections seem to indicate that the operation can be done just as well from below the diaphragm as from above in at least 92 per cent of cases. In the 8 per cent of cases in which there are not discrete nerve trunks but multiple branching nerves, I think the best approach might be from above the diaphragm.

We should concentrate our thought on cases in which gastric neurectomy, not associated with other surgical procedures, has been performed in order that we may get the data required for adequate study and evaluation of the procedure.

# CARCINOMA OF THE COLON<sup>1</sup>

EFFECT OF RECENT ADVANCES ON THE SURGICAL MANAGEMENT

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IN THREE PREVIOUS REPORTS,<sup>1,3</sup> we have discussed the management of cancer of the large intestine. These have reviewed our personal experience in this field of surgery and outlined the methods of preparation and operation that seemed, at the time, to offer the best chance for a favorable outcome. It is now our intention to present the data on 105 additional patients observed and treated since January 1, 1943. With advances in the preparation of patients for operation, better anesthesia, changes in surgical technic, and more physiologic after-care and experience, there has come about a naturally-expected improvement in immediate results. It is not our intention to discuss, in this communication, carcinoma of the rectum that because of location and extent has required combined abdomino-perineal operations. We will, however, include all cases which have been operated upon by the abdominal approach only, in spite of the fact that some of these with pelvic anastomosis would have been subjected to a combined procedure in our earlier reports. Actually, some of these high rectal, rectosigmoid, and low sigmoid lesions will be considered in this paper in one group and only those needing complete extirpation of the rectum excluded.

We have been disturbed by the trend of the times, indicating a great revival of interest in operations upon the rectum that include preservation of the anal sphincter.<sup>4</sup> This tendency is growing, and is the natural result of two main factors. One is the work of Gilchrist and David,<sup>5</sup> and that of Collier, *et al*.<sup>6</sup> Both groups having demonstrated that the initial spread of disease from the rectum and low colon is cephalward. It may be possible that when the spread of disease ceases to be in a cephalward direction that cure is unlikely. That we may safely have a shorter distal segment of normal tissue than is necessary on the proximal side is now accepted by all, since the lymphatic spread is so intimately associated with the blood supply to the region. It is obvious that surgeons, who have had considerable experience in this field, may well select their cases properly from the standpoint of the type of operation suitable, or justifiable, under given circumstances.

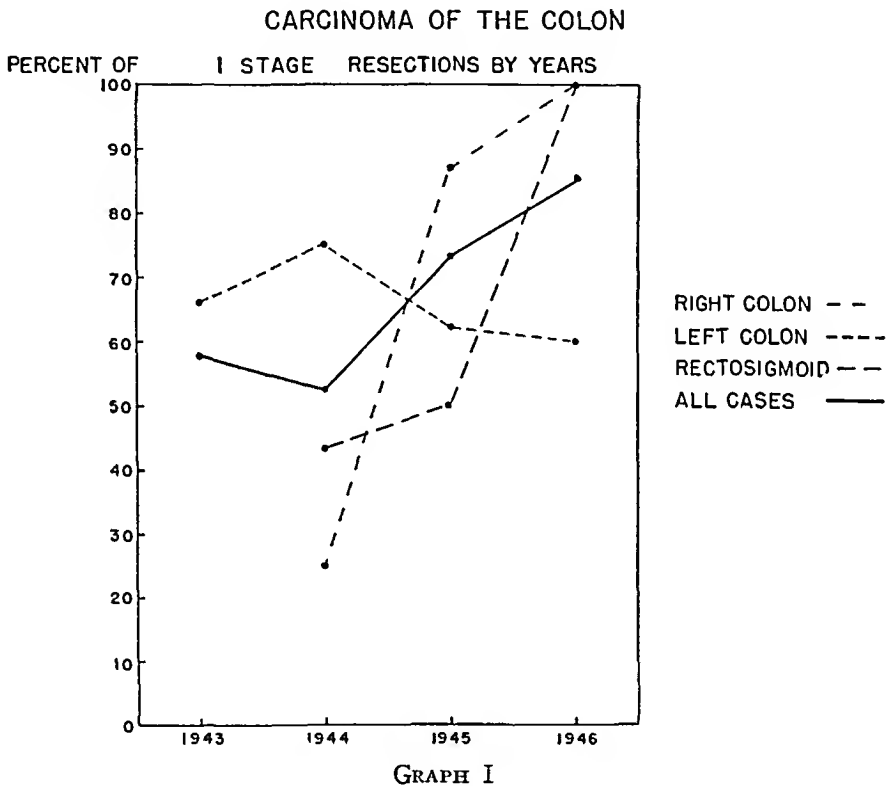
The second influence is the advancement in operative technic, preparation, and after-care. This leads to immediately-successful, though difficult procedures. However, one should emphasize the importance of cure rather than the relatively unimportant preservation of the sphincter. Our only

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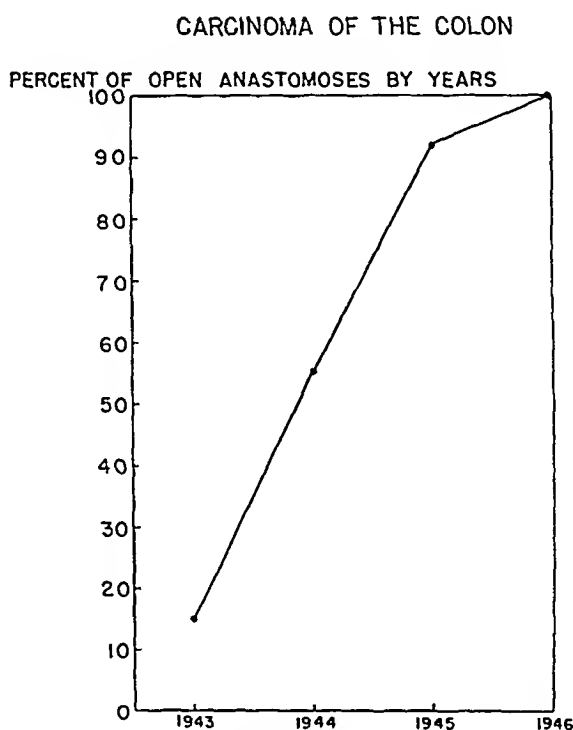
reason for bringing it into this discussion at all is to warn the enthusiastic, skillful, young surgeon that time will be needed to evaluate some of these procedures. We do know that local recurrences take place and that some of these might have been prevented if a complete operation had been undertaken. Also, it must be borne in mind that permanent colostomy is not incompatible with comfort and a normal life. The operation of Miles has become so standardized that, now, the risk is incredibly low. In 100 consecutive patients admitted to the wards of the Massachusetts General Hospital with cancer of the rectum, 72 were resectable and, of these, only two



failed to survive. Inasmuch as most of these operations were done by the resident staff, this mortality rate of less than 3 per cent is all the more striking. At this time, it seems obvious to us that the safety of this procedure with its applicability to contact spread of the disease should be taken into consideration in the selection of operation.

In the General Hospital, we<sup>2</sup> found that the ratio of admissions with carcinoma of the rectum to carcinoma of the colon was 2 to 1. This is not a true picture of the problem in our community, or according to vital statistics in the country at large. It appears that during the past three years, at least,

we have received into the private wards a reverse of this ratio. Perhaps, this may be influenced to some extent by a greater number of low anastomoses but, on the whole, may reflect somewhat on the type of the referring physician and the circumstances of the patient. A few years ago, it was apparent that more surgeons in this locality felt themselves competent to cope with carcinomas of the colon than with those requiring a combined operation. It seems obvious that this situation would, in time, change. Now, many of our patients with advanced disease of the colon and rectum have been explored and then referred to us if the extent of the process appeared formidable and the problem complex. Doubtless the fatalistic attitude concerning cancer of the bowel, formerly held by the layman, and too often



GRAPH II

accepted by the physician, is changing to a more hopeful outlook. It is discouraging, however, to find little evidence that much has been accomplished regarding earlier diagnosis. The average duration of symptoms in the group of carcinomas of the rectum referred to above was seven months.

#### RESECTABILITY

In our last report,<sup>3</sup> we favored the term resectability to that of operability. Inasmuch, as many of these lesions require the removal of adjoining structures with widespread local extensions or even liver metastasis where cure is impossible, it seems now that such an attitude is even more justifiable. The more advanced the lesion, the poorer the operative risk. On the other hand, it is incredible that the extent of some of these resections, including many

contact organs, is compatible with immediate success. Occasionally the respite is a short one but frequently it is of years duration. The physical and mental comfort to the patient is definitely worth the effort expended. Palliative procedures that fail to remove the primary lesion are much less satisfactory, although we question the effect on regression of metastatic disease by removal of the primary focus.

In our previously reported series, the resectability rate was 91 per cent. In the present group, it was 95 per cent. This indicates that perhaps we have been fortunate in the effect of earlier diagnosis to some extent in our community. However, the large number of cases with extensive disease is discouraging. We do not believe that we have included a greater number of resections of adjacent contact structures in this group than in the former

#### MORBIDITY

The period of invalidism following colon resections is dependent on many factors. In spite of the often two-stage attack that is necessary in the presence of acute obstruction, the final resection followed by primary anastomosis has been more satisfactory in our hands than exteriorization procedures. Although advocates of Mikulicz's type of operation with their increased experience have met the situation with a reasonable mortality rate, the actual number of hospital days has usually been increased. It is interesting that frequent reports are now appearing, suggesting a more widespread adoption of primary anastomosis.

Previously, we have felt that proximal decompression, either before or at the time of primary anastomosis, was an additional safeguard to the patient. Since the introduction of the Miller-Abbott tube and the use of sulfasuxidine and sulfathalidine in the preparation of patients for colon resections, fewer have needed cecostomy. We still use it in acute complete obstruction and, on occasion, supplement this procedure with complete transverse colostomy. This latter type of decompression is particularly adaptable to extensive inflammatory reaction about the initial lesion. Although rarely necessary in preparation of patients with cancer of the left colon, it is justifiable in doubtful cases and is essential in diverticulitis with obstruction or abscess formation.

When staged procedures of any kind are done, the convalescent period must include all the necessary hospital days whether or not there is an interim at home before the final closure of the temporary decompression. Tube cecostomies, such as we use, heal spontaneously in most instances. We feel, however, that complete colostomies are best handled by final excision of all scar tissue and an accurate end-to-end anastomosis with the bowel dropped free into the peritoneal cavity. Closure of colostomies within the abdominal wall has not been popular in our clinic, even if successful, the patient often complains of discomfort where the bowel is fixed in the abdominal wall. This is particularly true of the transverse colostomy most often used by us. It is of interest that exact anastomosis of the transverse colon, replaced within the peritoneal cavity, has not resulted fatally in any case in our hands.

# CARCINOMA OF COLON

## MORTALITY

Deaths following operations upon the colon that occur in the hospital have been taken as the basis for determining the operative mortality. Inasmuch as many of these patients are aged and depleted from other diseases, there will of necessity be deaths from causes unrelated to the operative procedures. These however must be included, since few of these patients have anything else the matter with them and, if unrelated deaths were excluded, there would be no sound basis on which to determine our immediate results. With the increasing advances in our knowledge concerning the physiologic principles upon which life depends, there has been a steady decrease in operative mortality. The added benefits of chemotherapy have doubtless played a rôle, but we believe too much credit has gone in this direction.

TABLE I  
CARCINOMA OF THE COLON

Years	No of Cases	Resectability %	Resection Mortality %
1925-1942	143	91	17.5
1943-1946	105	95	2.0

TABLE II  
CARCINOMA OF THE COLON

	1943-1946	No of Cases	Deaths
Resections			
For cure	.	87	0
Palliative		13	2
Nonresectable		5	2
		<hr/> 105	<hr/> 4

Carefully controlled anesthesia, blood replacement, and better technical surgery, have really been the chief reasons for better results in our opinion. It is incredible how much surgery these depleted, aged patients with numerous complications will stand if properly supported.

In our previous series of resectable lesions, the over-all mortality rate was 17.5 per cent. In the present group of 100 patients two failed to survive a resection, a mortality rate of two per cent. Divided into groups of those with right and proximal transverse carcinomas one died, and of the left colon lesions two died. Two of the five nonresectable lesions, both in the left colon, failed to survive. During this interim 38 additional patients were subjected to abdomino-perineal resections for cancer, with one death. An additional 37 colectomies were performed for inflammatory processes, with two deaths. The improvement in results lead us to certain deductions relative to the preparation of the patient, the type of anesthesia, details of the operative procedure, and the after-care. Various modifications of routine measures were necessary according to the situation found.

## PRELIMINARY PROCEDURES

In the presence of acute obstruction, one has little time to improve the patient's condition until this feature has been overcome. In cancer of the right colon, obstruction usually comes as a late manifestation, and more often represents an inoperable situation. These are, however, frequently associated with an incompetent ileocecal valve and, in a few instances, with intussusception in an otherwise easily resected tumor. Decompression by the Miller-Abbott or Harris tube is often effective enough under these circumstances to allow an early attack on the site of involvement. When the plain film of the abdomen reveals dilated coils of small intestine, one may reasonably expect the long tube to produce adequate preliminary drainage. If this fails, or if the distention is not proximal to the cecum, then an early ileotransverse colostomy is indicated. This, we believe, is best done in continuity and, since the bowel cannot be previously prepared, should be accomplished by an aseptic technic. It is important to select as points for the anastomosis, the ileum 12, or more, inches proximal to the ileocecal valve and the midtransverse colon.

When the obstructed segment is in the left half of the colon, we believe that the safest and most effective immediate relief comes with a large tube cecostomy. Frequently such a procedure must be done as an emergency, since the cecum becomes avascular from prolonged distention and ruptures through a gangrenous spot, producing a fatal peritonitis. A suction trochar is effective in releasing enough gas and liquid contents to allow the semi-collapsed cecum to be exteriorized sufficiently for completion of the cecostomy without peritoneal contamination.

Rarely does one find the patient's condition suitable for an attack on the primary lesion in the presence of complete obstruction. We have occasionally accomplished complete transverse colostomy when this segment was not too distended and when the diagnosis between cancer and diverticulitis was not clear. Exteriorization procedures in the presence of complete acute obstruction are to be condemned. The patient is not in condition to withstand the necessary dissection for an adequate cancer operation under these circumstances.

Explorations of the abdomen in the presence of acute large bowel obstruction are dangerous. Manipulation of the obstructed lesion will often result in fatal peritonitis. It should be emphasized that if a decompression is decided upon at exploration, it should be accomplished as far from the field of final attack as possible. Too many cecostomies have been established in the midline or even in the left side of the abdomen.

On admission a patient with suspected cancer of the colon should have the following studies in addition to a careful physical examination and history. A plain film of the abdomen will often reveal the approximate site of the lesion by the gas-pattern. This is particularly true when obstruction of any degree is present. If this fails to give a lead, one should then proceed with a careful sigmoidoscopy. Failing to visualize the lesion, barium enema must be resorted to, with complete understanding of the problem by the Roentgenol-

# CARCINOMA OF COLON

ogist The ease with which barium may flow from below through an obstructive area often tempts the examiner to fill the entire colon. On occasion, this complicates the situation to change the entire problem from one of simplicity to one of considerable hazard. It is true that the valve-like action near the growth may allow comparatively complete evacuation in the normal direction with absolute occlusion to the flow of barium from below. When such is the case, we get the least harm and the greatest aid from this type of examination.

The patient's anemia and electrolyte balance are evaluated and proper therapy is instituted to correct them. We have not been enthusiastic about catharsis in the preparation of the bowel for surgery. Although occasionally

TABLE III  
RESECTIONS OF COLON AND RECTUM  
Distribution of Cases 1943-1946

	Cases	Deaths
Carcinoma of colon	100	2
Carcinoma of colon (not resectable)	5	2
Carcinoma of rectum	38	1
Polyps of colon	9	0
Diverticulitis	14	2
Other diseases	14	0
Total	180	7

TABLE IV  
PORTIONS OF OTHER CONTACT ORGANS RESECTED IN  
PRIMARY CARCINOMA OF THE COLON  
1943-1946 100 Cases

Uterus and adnexa	10
Small intestine	3
Bladder	2
Abdominal wall	2
Stomach, duodenum, spleen, gallbladder, liver, kidney, seminal vesicles—each 1	7
	24

this works well, it more often fails in its accomplishment, and causes the patient a good deal of distress. Perforation and peritonitis may result from vigorous catharsis and enemata. Some individuals do well on small doses of mineral oil, particularly while waiting for admission to the hospital.

Since sulfasuxidine became available, we have been impressed by the value of this drug in its liquefying effect on the fecal contents of the bowel and we used this method of preparation until sulfathalidine was brought out for experimental trial. This latter drug is superior to sulfasuxidine because the remaining bowel contents stay in a semisolid state. This holds bacteria in a mass that is more easily controlled than is possible when the feces are liquid. We believe that sulfathalidine is as effective in the preparation of the

bowel for surgery as is sulfasuxidine. Also, we have not noted the occasional bleeding from the growth when this drug was used that we had observed when sulfasuxidine was in use. The recent finding of Poth, *et al*,<sup>7</sup> that sulfathalidine and penicillin were antagonistic must be borne in mind. The experimental evidence of Young and Cole<sup>8</sup> with the use of sulfathalidine and sulfasuxidine intraperitoneally is intriguing, and may be of value if further experience substantiates these views.

During the five to seven days required for suitable bowel preparation, the patient can be put into better condition to withstand surgery. It has not always been possible for us to completely correct the serum protein level by the methods at our disposal. This difficulty has usually been noted in those patients having secondary small bowel involvement. This is particularly true if fistula formation between the attached small intestine and the colon exists but may present a problem when partial obstruction of the small bowel is a

TABLE V  
AVERAGE HOSPITALIZATION  
Resection of Colon 1943-1946

	Preop Days	Postop Days	Total Days
One-stage operation	6 5	18 3	24 8
Two-stage operation			
Preliminary cecostomy	3 4	29	32 4
Prelim ilio-trans colostomy	5	33 3	38 3
Prelim trans colostomy	7 4	47 1	54 5

part of the picture. It has seemed to us that prolonged attempts to correct the deficiency states are often disappointing. Improvement beyond a certain point is often impossible and a persistence along these lines may lead to a poorer risk rather than a better one. The early favorable changes observed following the removal of an infected, obstructing lesion are spectacular. Such aids as blood, plasma, and amigen appear more effective postoperatively, although the patient's ability to utilize an unobstructed gastro-intestinal tract is probably the chief reason for this impression.

The choice of anesthesia should depend on the circumstances and experience of the surgeon and his anesthesia department. We prefer continuous drip procaine spinal anesthesia supplemented often with small amounts of pentothal sodium.<sup>9</sup> Since the adaptation of this method, we have observed little evidence of pulmonary complications. It must be admitted that chemotherapeutic agents, used primarily to prevent sepsis in the surgical areas, might well secondarily influence the incidence of pulmonary and bladder infections.

Incisions have varied to some extent depending on previous bowel drainage and the location of the tumor. In primary right colectomy, we have usually found a long right paramedian incision more satisfactory since this allows adequate exposure of the vascular source and nodal spread. Transverse incisions

are preferred for the flexures and the lesions involving the midcolon. The left colon exposures have been paramedian in cases where permanent colostomy might prove necessary. Oblique incisions with mesial retraction of the rectus muscle have been satisfactory for low sigmoid tumors suitable for end-to-end primary anastomosis. We have practiced delayed primary wound closure, as advocated by Collei and Valk<sup>10</sup> with a minimal of wound infection. Wounds have been closed in layers with No. 30 interrupted cotton and stay-sutures of heavy cotton for the skin and fat. Dehiscence has never been a serious problem, occurring only once in our experience, and this one was in a wound containing an end-colostomy.

Resection of the involved bowel and mesentery has been wide on the cephalward side in all instances. In left colon lesions, the distal segment has been adequate to include any extension of disease into the surrounding tissues. We have found that dividing the bowel between thin clamps in the proximal portion early in the procedure is of great advantage. This makes the remainder of the dissection easier because of better exposure. Instead of isolating named blood vessels to insure viability, we have removed the disease and then determined by visualization that the blood supply of the ends to be anastomosed was adequate. Contact structures are removed with the primary tumor *en bloc*. These have included all the nonvital organs, or parts of them, within the abdomen and pelvis.

Although we championed aseptic anastomosis by a modification of the Parker-Kerr technic in our earlier publications, we have more recently used the open method in all operations of election. Also, we have abandoned the two rows of fine catgut previously advocated. The reasons for our changes in technic have been based on the following factors. The aseptic methods of anastomosis, previously satisfactory in our hands, require considerable experience and a strict attention to detail. Since we were responsible for the teaching, by precept and example, of many resident and graduate students, it became obvious that some of them would have to learn the pitfalls of the method by their own experience. In addition to this, we had great difficulty in carrying out a strictly aseptic technic in some of the low anastomoses. We were further supported by the improvement in bowel preparation brought about by sulfasuxidine and sulfathalidine. By the careful avoidance of gross contamination and the discarding of instruments, drapes, and gloves used in the anastomosis, our results have been as good by this method as they were with the aseptic technic.

We now use an outer row of interrupted sutures of No. 30 cotton. They are placed posteriorly before the clamp is removed from the proximal segment, in all cases, and from the distal segment except when the rectum itself is to be used. We feel that even a thin-bladed clamp damages the nonperitonealized rectum too much to warrant its use in that location. We vary the type of suture used to considerable extent. Transverse mattress sutures are always used across the white lines of the bowel because of the failure of the Lembert suture to hold on these longitudinal fibers. The Halstead mattress suture has



only the advantage of fewer knots, and for this reason may be the choice except when location makes accurate placement difficult to achieve. An inner mucosal approximation is accomplished by very fine chromic catgut on an atraumatic needle. An over-and-over stitch or a locked variety is used posteriorly while the anterior margin is approximated by the Connell method. This technic of an outer row of nonabsorbable interrupted sutures has the advantage of no permanent constriction of the bowel at the point of union. A distended segment can be joined to a collapsed portion by the simple expediency of wider bites on the larger bowel. We have not found much advantage in oblique section of the colon ends, although this is helpful when dealing with the small intestine.<sup>11</sup>

The rent in the mesentery is carefully closed on both sides when the anastomosis is completely within the peritoneal cavity. If a pelvic dissection has been necessary, we leave the lateral margin between the bowel and pelvic peritoneum open. This obviates the necessity of draining this region, as formerly practiced, through the ischial fossa. Fistula formation with resultant stenosis of the suture line is thereby avoided. Collections of serum in the hollow of the sacrum may burst into the peritoneal cavity with a transient intraperitoneal reaction. As a rule, however, seepage from this space is gradual and is adequately handled by the peritoneal cavity. We have had only one fatality in low anastomoses. This was undertaken in an elderly man, with an extensive growth and liver metastases. On the 18th postoperative day, an enema was given by error. Immediate signs of peritonitis resulted in death five days later from fulminating gas bacillus infection throughout the abdomen. At post-mortem, the suture line was intact but an abscess in the hollow of the sacrum had ruptured, to produce the sequela described above. We doubt that concomitant drainage of the pelvis at the time of the original procedure would have brought about a happier result. This opinion is based on our earlier experience with this region when drainage through the ischial fossa was the rule.

We have given up local use of sulfonamides either into the peritoneal cavity or within the wound. It may be that the use of sulfasuxidine or sulfathalidine, as suggested by Young and Cole,<sup>8</sup> may prove of benefit when gross contamination by fecal matter has occurred. These investigators find that the above drugs are very rapidly absorbed from the peritoneal cavity, with little evidence of intestinal adhesions in their experimental animals. Sometimes we have used penicillin intraperitoneally, but are not convinced of its better effect when so administered. If there is no contraindication to sulfonamides, we use sulfadiazine intravenously during and immediately following the operation. Penicillin is substituted for sulfadiazine if the latter may appear to be hazardous. Streptomycin has been used occasionally.

All patients are given enough whole blood to replace that lost during the operation. Further transfusions are given if the blood and protein level of the serum have not been brought within normal range before operation.

Preliminary cecostomy or colostomy are used only in the presence of complete obstruction. Concomitant cecostomy has been abandoned. In

patients with left colon lesions admitted with acute obstruction, a large tube cecostomy is done as an emergency procedure by a method previously published by us<sup>1,2</sup> Recently, Millet,<sup>1</sup> in our clinic, has devised an ingenious method of cleansing the colon through a previously-placed cecostomy. He inserts a Miller-Abbott tube through a rent in the anterior surface of the rubber arm, leading from the right-angle glass tube used to prevent kinking in the abdominal wall. Complete flushing of the colon is thereby obtained. Salt solution is introduced through one lumen and removed by suction through the other. Suspensions of sulfathiazidine can be substituted for saline solution after the cleansing process has become well-established. Inasmuch as the end of the Miller-Abbott tube reaches the point of obstruction by peristalsis, it is very effective even if the colon has inadvertently been filled with barium by an over-enthusiastic Roentgenologist. Millet's method appears, at this time, to be so simple and thorough that preliminary transverse colostomy may be rarely needed in the future. It is of importance however that the preliminary cecostomy be made in a manner suitable for the introduction of the double-lumen tube through it.

Patients are kept mobilized if possible until the day of operation. Some of them can practice early postoperative ambulation. The majority of this group of cases, however, are not candidates for early rising in its true sense of the word. In suitable patients, we used dicoumarol postoperatively to prevent venous thrombosis. Many of them, on the other hand, are arteriosclerotic or have other contraindications to the anticoagulant drugs. In these, we practice prophylactic superficial femoral vein interruption. If the lesion is well above the pelvic floor, this procedure can be done before, or at the time of, the bowel resection. If, however, pelvic dissection is necessary, then the vein interruption should be postponed for 48 hours after operation. There is a transient engorgement of the pelvic veins immediately following femoral vein interruption that definitely increases the blood loss during the pelvic dissection. Since prophylactic vein interruption has been carried out in 458 elderly patients in our hospital without harm, we believe it is a reasonable safeguard against thrombophlebitis and pulmonary embolism.

The average hospital stay in this series of cases was 32.4 days. The average number of days preoperatively was six days. There were 26 cases requiring preliminary bowel drainage or some two-stage procedures. These averaged 39.9 days in the hospital, while those requiring no second stage averaged 24.8 days. The lack of proper home facilities or the distance necessary to travel influenced to some extent the duration of hospital stay.

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DISCUSSION—DR WARREN H COLE, Chicago, Ill These figures of Doctor Allen's revealing no deaths following resection in 87 cases of curable carcinoma of the colon are excellent, but I am afraid that anyone who has had such a large series without a death will have one, even though it is due to something as unexpected as plaster falling from the ceiling upon a patient I am glad he has emphasized the advisability of a two-stage resection in a large percentage of patients with carcinoma on the left side (where obstruction is so common), because the tendency to switch toward a one-stage resection is bound to go too far, and we will lose patients who should have had a two-stage operation I make this statement largely because I work in a charity hospital where the great majority of our patients with carcinoma of the left colon have at least a partial obstruction, many have complete obstruction It is not safe to consider a one-stage procedure in that group

I was glad to hear Doctor Allen say he was doing most of his cases with open technic I am firmly convinced that this is safe, particularly with the use of sulfasuxidine or sulfathaladine by mouth preceding operation I do not know what he thinks about these drugs, but I personally feel they have great merit and will help us obtain a smoother convalescence, and a lower mortality rate

DR ARTHUR W ALLEN, Boston, Mass I would like Doctor Cole to answer one question He has advocated intraperitoneal use of sulfasuxidine and sulfathaladine, and I should like to know how he feels about it at this time

DR, WARREN H COLE, Chicago, Ill I did not mention intraperitoneal use of sulfasuxidine and sulfathaladine because streptomycin may have made that procedure obsolete We used one of these drugs (6 Gm intraperitoneally) in every case of colon resection until streptomycin became available I was convinced that it helped in lowering complications When placed in the peritoneal cavity either of these drugs is absorbed rapidly but it is not absorbed from the wound, their use must be limited to the peritoneal cavity Absorption is not quite so rapid as with sulfanilamide, but much more rapid than with sulfathiazole or sulfadiazine, these drugs produce no adhesive reaction, as is occasionally noted with the latter two drugs Since sulfasuxidine and sulfathaladine are so effective in limiting the growth of *B coli* in the lumen of the large bowel, it appears logical to expect a similar action in the peritoneal cavity when large bowel contamination has taken place

# THE PERSISTENCE OF SYMPTOMS FOLLOWING CHOLECYSTECTOMY<sup>\*</sup>

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THE RECOGNITION of a definite syndrome associated with disease of the biliary tract, particularly calculi, extends back hundreds of years. Aggressive treatment of this syndrome, however, is hardly 75 years old. Surgical attention was first directed at the removal of stones from the gallbladder, with the operation of cholecystostomy. This was followed shortly afterward by extirpation of the gallbladder, and in a relatively short period of time both of these procedures were being performed with sufficient safety to warrant their inclusion in the armamentarium of the surgeons.

As cholecystostomy and cholecystectomy became more frequently performed, it was possible to evaluate the efficacy of each, and this was done by frequent reports of large series of cases studied statistically. This was an expensive method, yet proved to be an effective one. Fairly early, it became obvious that the results obtained in simple drainage of the gallbladder in patients with chronic cholecystitis were not nearly so satisfactory as those that followed cholecystectomy. This latter operation, therefore, has, during the years, become the procedure of choice, and one seldom encounters anyone advocating cholecystostomy except in the occasional case of acute involvement of the gallbladder where the surgeon thinks that cholecystectomy at that time would be too formidable a procedure for the patient. It also became possible to prognosticate, with a considerable degree of surety, the particular patient who would be relieved of his distress following cholecystectomy. While there have been many contributions on this phase of the subject, the papers of Judd,<sup>1</sup> Whipple,<sup>2</sup> Mueller,<sup>3</sup> Finsteier,<sup>4</sup> Elman,<sup>5</sup> and Parsons,<sup>6</sup> are adequate. Where stones are present in the gallbladder and where the patient gives a history of typical biliary colic on several occasions, and where there is a history of nausea, vomiting and dyspepsia, one can usually anticipate a successful outcome. If to this history is added the physical finding of tenderness in the region of the gallbladder and the radiologic finding of nonvisualization of the gallbladder with cholecystography, or the presence of stones, the surgeon can usually anticipate that from 80 to 95 per cent of his patients will be relieved of their symptoms following cholecystectomy.

In the stoneless gallbladder, the results have not been so satisfactory. With the advent of cholecystography and the ability to detect slight functional damage in the gallbladder, it was hoped that early cholecystectomy, in such

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<sup>\*</sup> Read before the 58th Annual Session of the Southern Surgical Association, Hot Springs, Va., December 12, 1946.

individuals, would offer a definite therapeutic advance. This has not proved to be the case. In a study by Graham and Mackey,<sup>7</sup> it was shown that where typical biliary colic was not an important feature in a patient with a stoneless gallbladder, cholecystectomy was doomed to failure in as high as 40 per cent of the instances. In that study, they made the interesting observation, which has been noted by others, that the relief of the symptoms of cholecystitis in the stoneless gallbladder was in almost direct proportion to the amount of damage present in the gallbladder wall. The greatest relief of symptoms was obtained in those patients in whom the gallbladder wall was thickened by virtue of fibrous tissue, edema and cellular infiltration, whereas those patients with relatively thin, normal looking gallbladder walls were for the most part destined not to be relieved of their symptoms unless stones were present. The failure of the concentrating ability of the gallbladder to function as determined by cholecystographic study, therefore, was not in itself an indication for cholecystectomy, and, thus, by inference the loss of function of the gallbladder was probably not the origin of the symptoms seen in the classical form of cholecystitis.

While cholecystectomy in the properly selected patient is one of the most satisfactory of abdominal operations, it is performed frequently enough for the relatively small percentage of unimproved patients to be a serious clinical problem. As a result there have been many reported studies as to why these symptoms persist and many suggestions have been offered as to their proper care. While no attempt will be made to review all of these reports, it is well that previous approaches be considered.

In our discussion we shall exclude those patients in whom other lesions, obviously responsible for the postoperative disability, can be demonstrated. Prominent among such causes are found peptic ulcers, duodenal diverticula with ampullary obstruction, diaphragmatic hernia, spinal nerve lesions, and the like. A certain number of patients will also show the persistence of stones in the common bile duct or in the stump of the cystic duct. Here the cause of the symptoms is obvious. Others will show traumatic damage to the common bile duct, and here, again, the solution to the problem is usually clear. After such patients have been excluded, there will still remain a considerable group in which careful review of the preoperative history and findings fail to add further information. As Elman<sup>5</sup> has pointed out, if some of these patients are studied during the period of intense colic for the concentration of amylase in their blood, this will often be found elevated. A high amylase value which falls rapidly to normal with subsidence of the acute attack is generally diagnostic of an acute episode of interstitial pancreatitis. It is important, therefore, that such determinations be made preoperatively, if possible, during the attack of so-called biliary colic. While this lesion is frequently associated with cholecystitis, it is well for the surgeon to be warned beforehand of the associated pancreatic involvement.

Residual biliary tract infection has been suggested as one of the common causes for the persistence of symptoms. This explanation would seem to be

of doubtful value. As has been pointed out, patients with noncalculus cholecystitis and cholangitis is often relatively free from severe pain, and one may frequently encounter various types of infectious hepatitis in which there is no pain at all, and, indeed, very little dyspepsia

Distortion, due to adherence of the duodenum or the pyloric region of the stomach to the gallbladder bed region, has, likewise, been suggested as an origin of the difficulties. Release of such adhesion, however, rarely relieves the individual. In operations upon the common bile duct that has become strictured as a result of previous traumatic injury, one is frequently surprised to note the extensive fixation of the duodenum to the liver and even to the anterior abdominal wall, with relatively few dyspeptic symptoms

One of the most common explanations referred to regarding the persistence of symptoms following cholecystectomy is that of biliary dyskinesia. The subject has been adequately reviewed by Ivy and Sandbloom<sup>8</sup>. This concept has to do chiefly with the mechanism of the choledochoduodenal sphincter and its neuromuscular relationship to the remainder of the biliary apparatus and the duodenum. While a functional spasm of this sphincter had been previously suggested by others, the experimental work of Westphal<sup>9</sup> gave great impetus to further observations. Westphal, working on guinea-pigs, brought out the fact that moderate stimulation of the vagus nerve below the diaphragm with a weak electrical current would produce contraction of the gallbladder, peristaltic motion in the antral portion of the sphincter of Oddi, and relaxation of the papilla. He looked upon this as the normal response. If the current was made slightly stronger, gallbladder contraction became greater, and peristaltic movements into the ampulla were also greatly increased. When a still stronger current was used, he noted that with the strong contraction of the gallbladder there was a spasm of the antral sphincter. He also noted that upon stimulation of the splanchnic nerve, the gallbladder and the antral portion of the sphincter relaxed while the sphincter of the papilla contracted. This he called atonic dyskinesia in contradistinction to the previously mentioned type, which was hyperkinetic dyskinesia. This led him to a rather elaborate classification of the operations of this physiologic mechanism, much of which has not been confirmed in the human. It was felt by Ivy and Sandbloom in their report that this choledochoduodenal mechanism could contract with sufficient force to prevent the evacuation of the contracted gallbladder and that by so doing, the resulting back pressure would be adequate to produce pain even in the non-inflamed biliary passage. Just how important a factor such as dyskinesia may be in clinical cholecystitis need not concern us here. Following removal of the gallbladder there is some question as to whether the rôle played by the sphincter of Oddi and the mechanism of reciprocal innervation is a dominant one. Weir and Snell<sup>10</sup> have suggested that it might be important. They have pointed out that there may be instances in which some abnormality of the sympathetic or parasympathetic innervation may produce spasm or increase in tone of the sphincter of Oddi which could produce sufficient back pressure and distention of the common bile duct to cause pain. That colicky pain associated

with nausea and vomiting can be produced from sudden distention of the common bile duct has been demonstrated in the human by Zollinger,<sup>11</sup> who placed a small balloon in the common bile duct at operation and rapidly inflated it. The demonstration of a true sphincteric spasm in the human, however, is not too clear-cut. Puestow<sup>12</sup> has offered evidence that exactly the opposite occurs following cholecystectomy. By transplanting fragments of the duodenum containing the intramural portion of the choledochus and the ampulla of Vater to the surface of the abdomen of animals, he made direct observations of bile flow, and came to the conclusion that cholecystectomy produced a loss of sphincter tonus and a more or less constant flow of bile. He explained the evidence offered by others of increased pressure within the common bile duct following cholecystectomy as being due to determinations made too soon after operation, while edema was still present in the ampullary region. In most of the clinical and experimental observations that have been made, it is difficult to exclude the effect of the duodenal musculature. It is our observation, on unreported experiments, that when the vagus nerve of a dog is stimulated in the neck with a strong electric current, not only is there contraction of the gallbladder and the duct musculature but of the duodenal wall as well. This latter muscle is so much more powerful than the sphincteric mechanism of Oddi that it might very easily offset the effect of any contrary innervations that might be present.

Another explanation for postcholecystectomy colic and dyspepsia that has been offered relates to the dilatation of the choledochus that is seen so frequently following cholecystectomy. This is an old observation, and yet the explanation is not too clear-cut as to why it should occur. Some of the evidence offered is still controversial. Puestow was unable to note any considerable enlargement of the choledochus when it was associated with untreated cholecystic disease. Benson,<sup>13</sup> on the other hand, in necropsy studies, found that in mild gallbladder disease without cholecystectomy there was a 32 per cent increase in diameter, while in severe gallbladder disease this increase was on an average of 64 per cent. Practically all observers agree, however, that in the majority of instances following cholecystectomy for gallbladder disease there is a considerable increase in diameter of the choledochus. The most common explanation offered for this observation is related to a loss of the water-absorbing mechanism that exists in the gallbladder, resulting in considerable back pressure. Another explanation that has been advanced is that it is the result of duodenal regurgitation. Puestow concludes that following cholecystectomy there is a permanent dilatation of the choledochus, but that there is no satisfactory explanation at the present time for this dilatation. He feels that it is usually associated with a low intraductal pressure and, therefore, tension within the choledochus is probably not responsible for postoperative symptoms. The observations of Benson, again, are of interest in this respect. He studied a number of patients coming to necropsy several years after cholecystectomy in order to determine the relationship between dilatation of the duct to the postcholecystectomy distress

Where such distress was found only 14 per cent showed normal-appearing ducts, while 86 per cent were markedly dilated. Of those patients who had no postoperative abdominal symptoms, 83 per cent of the bile ducts were normal in diameter, while only 17 per cent were markedly dilated. He feels, therefore, that distress after cholecystectomy is closely related to dilatation of the bile duct, and that this latter phenomenon is due to the loss of the absorptive function of the gallbladder and to the subsequent rise in pressure within the duct system. These observations correlate with the experiments of Schriager and Ivy,<sup>14</sup> and Davis, Hart and Cram,<sup>15</sup> who found that distention of the cystic duct and bile ducts in dogs was associated with pain, nausea (salivation) and vomiting. Butsch, McGowan, and Walters<sup>16</sup> have demonstrated that when a T-tube is inserted into the common bile duct after cholecystectomy and manometric determinations made of the intraductal pressure, this pressure can be made to rise with the administration of certain drugs, such as morphine. In one of the cases studied, this rise in pressure was accompanied by pain. They also noted periodic rises in pressure, with pain at times independent of the effect of morphine. Conversely, they were able to demonstrate that relaxation produced by amyl nitrite and glyceryl trinitrite relieved the pain concomitantly with the fall in intraductal pressure. A similar observation has been made independently by Doubilet and Colp.<sup>17</sup> It is also a common clinical observation, not supported by observations of intraductal pressure, that the pain in postcholecystectomy colic can frequently be relieved by the administration of glyceryl trinitrite.

One final observation must be considered as relating definitely to the association of symptoms following removal of gallbladder, namely, the persistence of a large portion of the cystic duct. This occasionally increases in size, so that it mimics a reformed gallbladder. Frequently the wall is thickened and a small stone is present. Often, however, this remnant of the cystic duct will not contain stones, and occasionally the wall has the thickness generally associated with a normal viscus. The removal of such a cystic duct stump has frequently resulted in the relief of symptoms, as has been pointed out by Beye,<sup>18</sup> and Gray and Sharp.<sup>19</sup> Strangely enough, there has been but little comment on the mechanism by which the remnant of a cystic duct can produce symptoms identical to those of biliary colic, and why these symptoms will be relieved following the removal of the duct. The presence or absence of stones seems to make but little difference in the end-result.

From the above considerations, it would seem that some common denominator must be sought for, in which an explanation of the relief of symptoms from the removal of the stump of the cystic duct, or the relief of tension in the common bile duct, or the probable relief of spasm of a choledochal sphincter might correlate. Since the symptoms under discussion in the so-called postcholecystectomy syndrome resemble identically those of cholecystitis and cholelithiasis, it would seem to us that such explanations as are offered must also correlate with the cause of symptoms seen in the usual case of cholecystitis.



Recently,<sup>20</sup> we had occasion to report on certain observations relating to the production of symptoms of cholecystitis. Because of the fact that the symptoms commonly observed in cholecystitis, such as pain, nausea, vomiting, and dyspepsia, are symptoms that can best be explained on the basis of sympathetic and parasympathetic stimulation in the gallbladder region, we examined

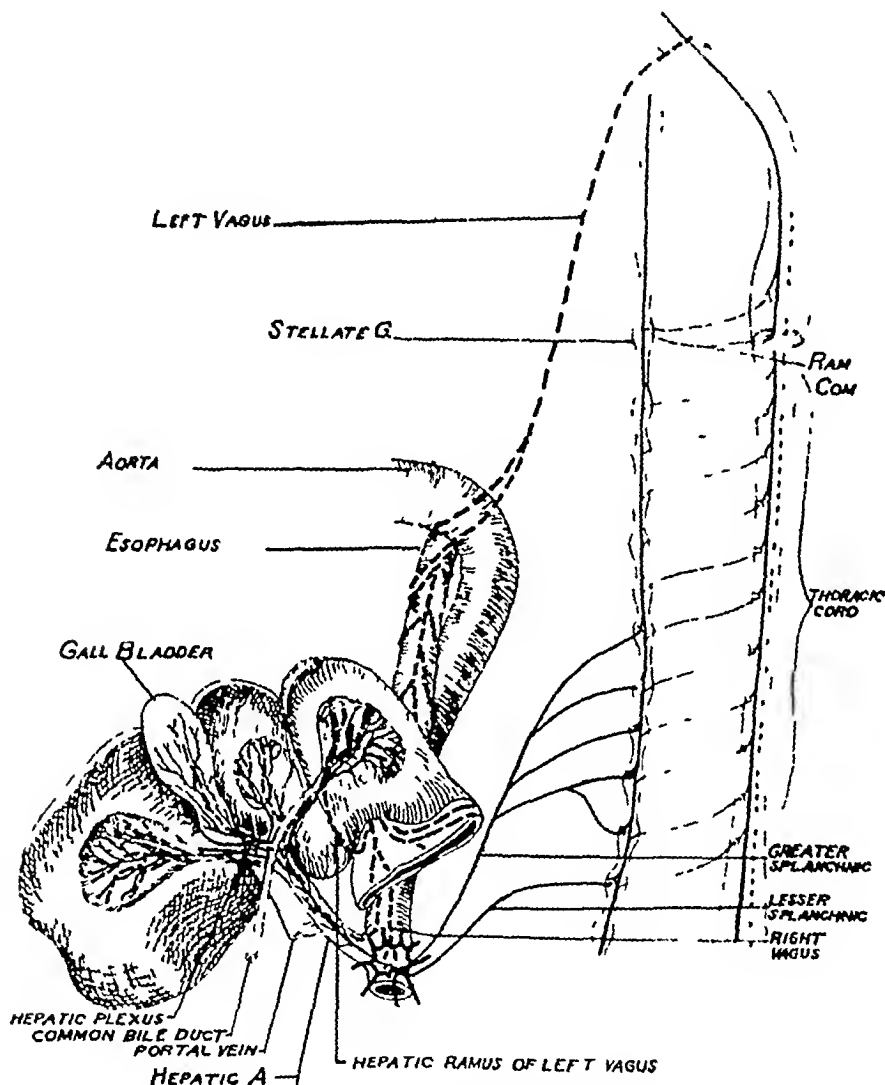


FIG 1—Diagrammatic representation of the origin and gross distribution of the sympathetic and vagus nerve supply to the biliary tract and liver (After Kuntz<sup>24</sup>)

the walls of diseased gallbladders to ascertain, if possible, whether any lesion could be demonstrated involving these nerve pathways. We were able to show that in chronic cholecystitis, in which there is generally seen marked inflammatory changes in the wall of the gallbladder and in which the patient exhibits a considerable amount of pain, nausea and vomiting, it is very easy to

demonstrate pathologic changes in and around the nerve fibers within the gallbladder wall. These changes, for the most part, consist of fibrosis and inflammation producing stretching, ischemia, and the local effect of inflammation around the nerve fibers and endings. These factors either actually produce pain or else so lower the threshold so that stimuli not normally apparent to the individual may result in marked symptoms. Following cholecystectomy

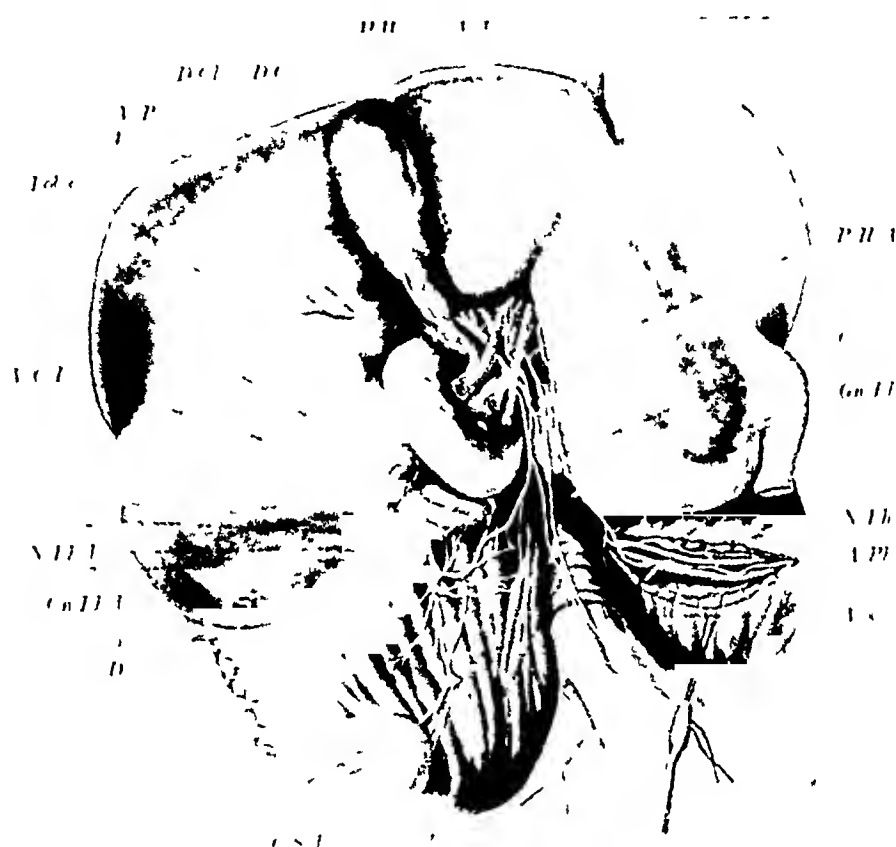


FIG 2—(A) Drawing prepared from dissection of an adult with the hepatoduodenal ligament removed and the liver raised to illustrate the distribution of the phrenic supply to the liver. VCI—inferior vena cava, cut through, Lob c—caudate lobe, D—diaphragm, G S d—right adrenal gland, A H—hepatic artery, D H—hepatic duct, V P—portal vein, A Ph s—left inferior phrenic artery, D C—cystic duct, N Ph d—right phrenic nerve, Gn Ph d—right phrenic ganglion, V s—left vagus, N Ph s—left phrenic nerve, Gn Ph s—left phrenic ganglion, 1—hepatic rami of the vagus nerve, 2—phrenic branches to the inferior vena cava, 3—branches to the posterior surface of the liver, 4—the branches in the portal area, 5—muscular branches, 6—the branches of the left phrenic nerve to the portal area. (After Raigorodsky<sup>22</sup>)

many nerve fibers, as well as the above mentioned lesions, are removed, and with this loss of a large number of nerve trunks along with the focus of stimulation, there is subsequent improvement in the clinical condition of the patient. These observations were demonstrated with characteristic photomicrographs observed on routine examination.

If these above mentioned observations are true, it would seem to us that a similar mechanism must be shown to be present in explanation of the existence of the same symptoms following cholecystectomy. This report concerns such a study of the nerve supply relating to the bile ducts. In view of

the fact that so little attention has been paid to the nerve supply to this region, we feel that it would be of value to describe first the anatomic distribution in detail

#### THE NERVE SUPPLY TO THE BILE DUCTS

The nerve supply of the liver and biliary system is derived from the sympathetic, the vagus, and the phrenic nerves. Dogiel<sup>21</sup> pointed out, in 1895, that the gallbladder and bile ducts, including the cystic and common ducts,

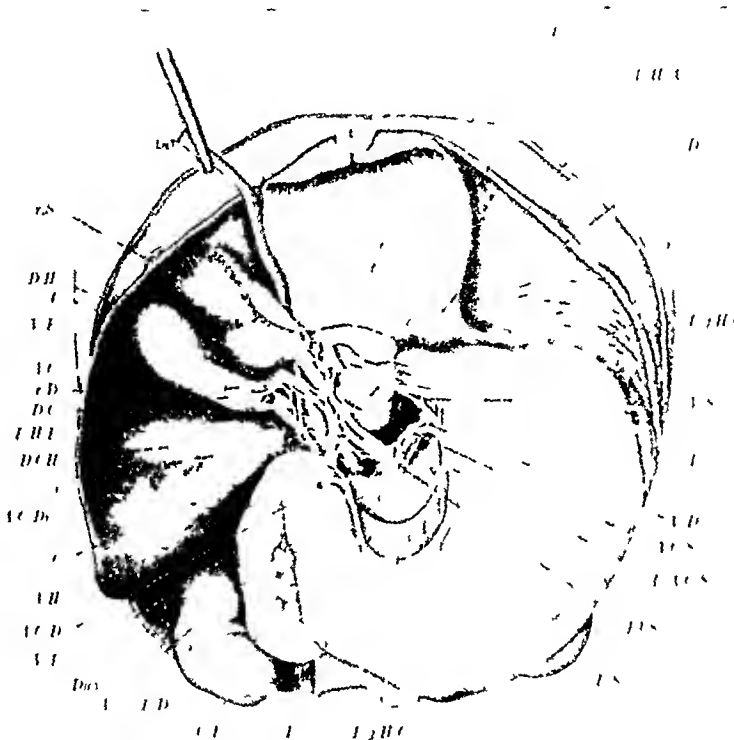


FIG 2—(B) Preparation as dissected from a child showing the more common type of arterial and nerve distribution. D—diaphragm, Lig HG—Lig hepatogastricum, L—spleen, RS—left kidney, Pn—pancreas, C Pn—head of the pancreas, RD—right kidney, Duo—duodenum, Lig t—ligamentum teres, VF—gallbladder, Ao—aorta, AH—hepatic artery, AG Duo—gastroduodenal artery, AGS—left gastric artery, AGD—right gastric artery, rS—left hepatic artery, rD—right hepatic artery, AC—cystic artery, PlS—solar plexus, PAGS—plexus of the left gastric artery, PHA—anterior hepatic plexus, PHP—posterior hepatic plexus, VS—left vagus, VD—right vagus, 1—hepatic branch of the left vagus, 2—branches to the liver, 3—branches to the anterior hepatic plexus, 4—medial nerve of the gallbladder, 5—posterior nerve of the common bile duct, 6—plexus of the gastroduodenal artery (After Raigorodsky<sup>22</sup>)

have a relatively rich nerve supply. A detailed study by Raigorodsky,<sup>22</sup> in 1928, in which he carefully dissected 60 human specimens, led to much clarification of the subject.

Figure 1 is a diagrammatic representation showing the pathways of the sympathetic and vagus nerve supplies to the liver and bile ducts. The left

vagus gives rise to three main branches as it passes through the lower thorax on the anterior surface of the esophagus. The right division is the hepatic branch, the middle and left being distributed to the stomach. The hepatic branch passes to the liver through the gastrohepatic ligament where it is joined by a branch of the right vagus. The distribution is almost entirely to the left lobe of the liver. As the right vagus passes along the posterior surface of the esophagus most of the fibers pass to the celiac ganglia, where a few

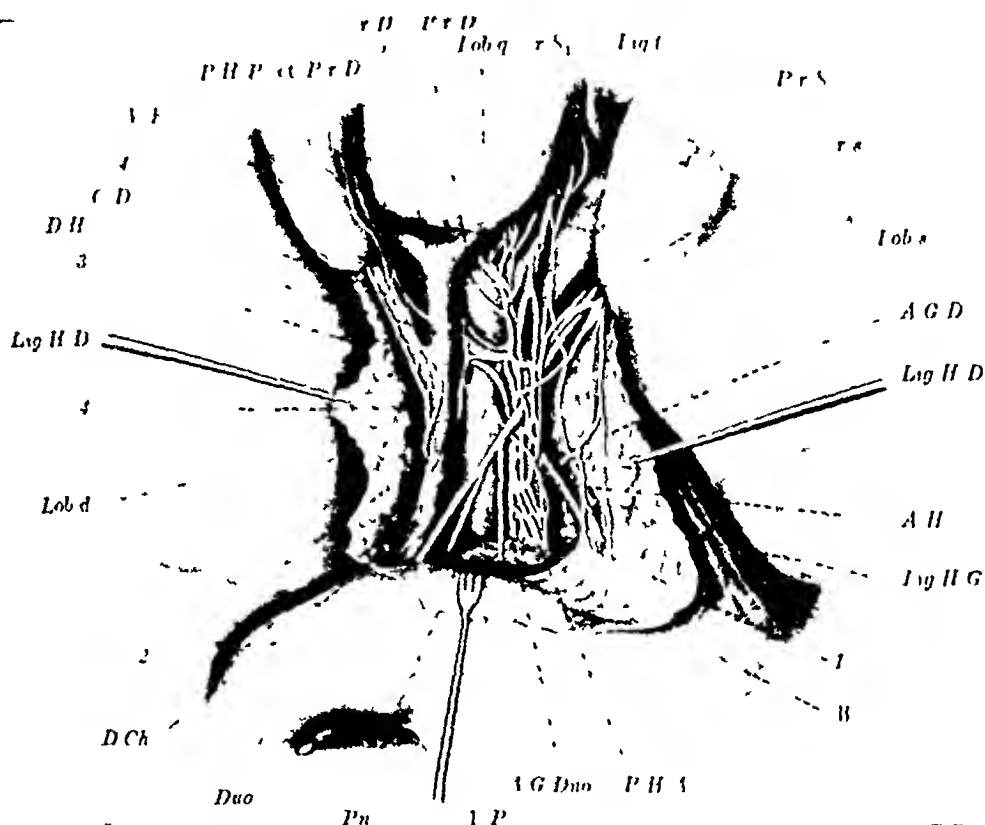


FIG 2—(C) Preparation of an adult with normal topographic relations seen from in front. Lob s—left lobe of liver, Lob d—right lobe of liver, Lob q—quadrate lobe of liver, Lig t—lig. teres, W—stomach, Duo—duodenum, Pn—pancreas, Lig H G—hepatogastric ligament, Lig H D—hepatoduodenal ligament, A H—common hepatic artery, A G D—gastroduodenal artery, r D—right branch of the hepatic artery, r s and r S1—left branch of the hepatic artery, V P—portal vein, P H A—anterior hepatic plexus, P H P—posterior hepatic plexus, 1—nerves with the right gastric artery, 2—anastomosis between the anterior and posterior hepatic plexus, 3—lateral nerve of the gallbladder, 4—cystic duct, 5—medial cystic nerve (After Raigorodsky<sup>22</sup>)

small branches become incorporated in the hepatic ramus and enter the hepatic portal. Eiger<sup>23</sup> (1916) considered the vagus to have the influence of a true secretory nerve on the liver.

The majority of the nerve fibers which are distributed to the biliary tree are derived from the sympathetic system, and reach the liver by way of the celiac plexus (Kuntz)<sup>24</sup>. These fibers are derived from the greater splanchnic nerves which have their origin predominantly from the T6-T9 sympathetic

ganglia, and the lesser splanchnics which arise from the T10-T12 sympathetic gangli. According to de Takats,<sup>25</sup> the greater splanchnic enters the superior portion of the celiac plexus, whereas a part of the lesser splanchnic joins the inferior pole, the majority being distributed to the renal and supra-renal plexuses. As has been pointed out by Greving<sup>26</sup> (1924), none of the



FIG 2—(D) Photograph of a dissection of the nerves of the portal area, as prepared by Raigorodsky<sup>22</sup>. The portal vein has been removed, and black silk has been placed behind the nerves for contrast. V—stomach, Pn—pancreas, Duo—duodenum, AGS—left gastric artery, vP—portal vein (cut end), vCI—inferior vena cava, DCh—common bile duct, DH—hepatic duct, PLS—solar plexus, PHA—anterior hepatic plexus, PHP—posterior hepatic plexus, PALS—plexus of left gastric artery, VS—left vagus, VD—right vagus, 1—hepatic ramus of left vagus, 2—branch from the right vagus, 3—branch from the plexus of the left gastric artery, 4—medial cystic nerve, 5—inner branch of the posterior nerve of the common duct, 6—posterior nerve of the common duct, 7—branch from the left vagus, 8—anastomosis between the anterior and posterior hepatic plexus, 9—pancreaticocholedochus nerve (After Raigorodsky<sup>22</sup>)

sympathetic rami join the liver directly from the sympathetic trunks in man, but first pass through the hepatic plexus

Figure 2-A is a drawing prepared by Raigorodsky showing the rami from the phrenic nerves to the liver. These fibers enter by first anastomosing with

the sympathetic nerves. This occurs predominantly along the posterior border, although some fibers enter through the hepatic portal.

The studies of Raigorodsky led him to divide the hepatic plexus, which is formed by the fibers approaching the liver from the celiac plexus, into anterior and posterior portions. The anterior hepatic plexus always follows the hepatic artery, the pathway changing as the path of the artery varies. The basic types of vessel differences correspond to the special pathways of nerves. Four basic types were originally described by Rio Branco.<sup>27</sup>

The most prevalent type occurs in 55 per cent of all cases (Fig 2-B and 2-C). The hepatic artery arises from the celiac axis and divides into two branches: the artery hepatica propria and the gastroduodenal artery. The hepatica propria artery divides into the right and left hepatic arteries, the right giving rise to the cystic artery just before it enters the liver.

The second type constitutes 20 per cent of the cases studied. The basic origin of the common hepatic artery is the same, but the right and left hepatic arteries arise directly from the common hepatic as separate branches without the formation of the hepatica propria artery. The cystic artery again arises from the right hepatic artery.

The third type is present in 10 per cent of the cases. The right hepatic distribution remains the same while the left hepatic artery arises as a separate branch from the left gastric artery.

The fourth type is found in 10 per cent of the cases also. The right hepatic artery arises as a separate branch from the superior mesenteric artery, passes behind the portal vein, and gives off the cystic artery just before entering the liver. The left gastric has the same type of basic pattern described in type one.

The other 5 per cent consists of variations and combinations of the above four basic types.

The posterior hepatic plexus of nerves passes to the right and superiorly in the portal area where at first it lies behind the lower third of the portal vein and crosses over on the under surface; it is then found lying in the outer groove between the right periphery of the portal vein and the common bile duct where it passes to the liver which it enters in the region of the end-branches of the right hepatic artery. Along the course of the right hepatic artery, it anastomoses with ramification of the anterior hepatic plexus.

The medial nerve of the gallbladder arises from the anterior plexus, passes over the anterior surface of the common and hepatic ducts, anastomoses with the posterior hepatic plexus in the triangle of the cystic and hepatic ducts, and passes to the medial superior surface of the gallbladder.

The lateral nerve of the gallbladder arises from the posterior plexus and passes along the lateral surface of the common and cystic bile ducts to the lateral, inferior surface of the gallbladder.

The pancreaticocholedochus nerve, as described by Laterjet,<sup>28</sup> is derived from the posterior hepatic plexus and passes distally to the retro- and intra-duodenal portions of the common bile duct.

The common duct is surrounded by a delicate net of nerve fibers throughout most of its extent. These fibers are much more numerous in the region of the junction of the hepatic and cystic ducts. The posterior surfaces of the cystic, hepatic, and common ducts are in close proximity to the posterior hepatic plexus which contains many large nerve fibers. Across the anterior surfaces of the hepatic, cystic, and common ducts pass many of the connecting branches between the anterior and posterior hepatic plexuses and the rami of origin of the medial nerve of the gallbladder.

Along the lateral inferior surface of the cystic duct is the lateral nerve of the gallbladder, while on the medial superior surface is the medial nerve of the gallbladder. As can be seen, one of the points of maximal concentration of nerve fibers along the biliary ducts is in the triangle formed by the cystic and hepatic ducts.

Labat<sup>29</sup> indicates that the gallbladder is insensitive, but that the bile ducts are very sensitive to tension of distention. However, Dogiel pointed out that nerve fiber bundles arising from the hepatic plexus accompany the blood vessels into the wall of the gallbladder and bile duct and form a plexus in the outer connective tissue layer from which fibers are distributed to the musculature and the mucosa. This plexus was described to contain many ganglion cells which occur singly or in groups. Greving (1924) was unable to confirm the presence of the ganglion cells in his preparations. We, however, have identified them on numerous occasions.

The sympathetic fibers probably make synaptic connection in the celiac ganglia. The connections of the vagus are not so well known, but the hepatic plexus may be the site of synapse, and if Dogiel is correct in his assumptions, the ganglion cells which he demonstrated were probably parasympathetic. As has been pointed out, some of the vagus fibers enter the liver directly. According to Kuntz, no anatomic data are available which prove that the efferent fibers in these branches effect synaptic connections with peripheral neurons. It is possible that some of these fibers are the axons of neurons located in the jugular or nodose ganglia.

The clinical observations of Kocher on cold injuries have shown, as early as 1896, that the vagi have no pain-carrying fibers from the abdomen (de Takats). As we have stated, it has been demonstrated experimentally by others that distention of the biliary ducts caused marked distress, disturbance in respiratory rhythm, salivation, and often vomiting. The symptoms produced were generally more marked with distention of the ducts than the gallbladder. Section of the right splanchnic nerve was found often to abolish the distress and reduce the amount of the respiratory inhibition. Section of both vagi and the left splanchnic nerve stopped the salivation and vomiting and reduced the amount of respiratory inhibition, while section of both vagi and both splanchnic nerves abolished all distress and reflex disturbances.

Reference has previously been made to the studies on a series of conscious patients made by Zollinger on the effects of distention of the gallbladder and bile ducts. Distention of the gallbladder was found to cause moderate

discomfort, no vomiting, and no referred pain. Distention of the cystic or common bile duct caused severe epigastric distress, vomiting in two of three cases and no referred pain. He considered this evidence in agreement with Morley<sup>30</sup> that a true visceral pain does exist which is mediated through the sympathetics and that inflammation of the peritoneum causes referred pain over a peritoneocutaneous reflex. Külenkampf, as reported by de Takats, emphasizes the fact that muscular rigidity will disappear with splanchnic anesthesia in colic if it is of reflex origin. However, if rigidity is due to peritoneal involvement resulting from the contiguous extension of the inflammation or to adhesions, the rigidity will not be influenced.

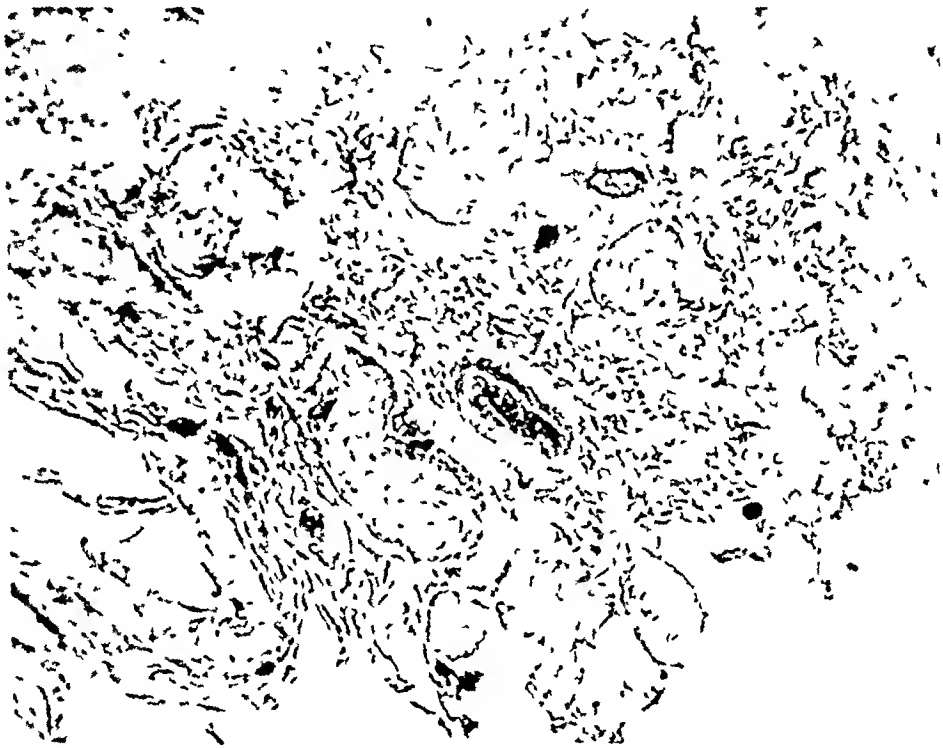


FIG. 3—Photograph of nerve fibers in section of the cystic duct taken just proximal to the point where the duct was clamped at operation. Other nerve fibers were present in each cross-section. These groups of fibers in each case possibly represent the medial or lateral nerves of the gallbladder after branching has taken place.

From the above observations, it seems logical to assume that stimulation of the sympathetic nerves in the portal area would cause epigastric pain and some disturbance in the respiratory rhythm, while stimulation of the vagus fibers in the same area would cause dyspepsia and in some cases vomiting.

In an effort to determine whether an appreciable amount of nerve fibers were cut during the average cholecystectomy, a consecutive series of gallbladders sent to the surgical pathology laboratory from Barnes Hospital were sectioned transversely through the cystic duct just proximal to the point where the clamp had been placed. Figure 3 shows nerve fibers which were found in this area. The nerve trunks can be seen to be quite small and numerous as



The common duct is surrounded by a delicate net of nerve fibers throughout most of its extent. These fibers are much more numerous in the region of the junction of the hepatic and cystic ducts. The posterior surfaces of the cystic, hepatic, and common ducts are in close proximity to the posterior hepatic plexus which contains many large nerve fibers. Across the anterior surfaces of the hepatic, cystic, and common ducts pass many of the connecting branches between the anterior and posterior hepatic plexuses and the ramus of origin of the medial nerve of the gallbladder.

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Labat<sup>29</sup> indicates that the gallbladder is insensitive, but that the bile ducts are very sensitive to tension of distention. However, Dogiel pointed out that nerve fiber bundles arising from the hepatic plexus accompany the blood vessels into the wall of the gallbladder and bile duct and form a plexus in the outer connective tissue layer from which fibers are distributed to the musculature and the mucosa. This plexus was described to contain many ganglion cells which occur singly or in groups. Gieving (1924) was unable to confirm the presence of the ganglion cells in his preparations. We, however, have identified them on numerous occasions.

The sympathetic fibers probably make synaptic connection in the celiac ganglia. The connections of the vagus are not so well known, but the hepatic plexus may be the site of synapse, and if Dogiel is correct in his assumptions, the ganglion cells which he demonstrated were probably parasympathetic. As has been pointed out, some of the vagus fibers enter the liver directly. According to Kuntz, no anatomic data are available which prove that the efferent fibers in these branches effect synaptic connections with peripheral neurons. It is possible that some of these fibers are the axons of neurons located in the jugular or nodose ganglia.

The clinical observations of Kocher on cold injuries have shown, as early as 1896, that the vagi have no pain-carrying fibers from the abdomen (de Takats). As we have stated, it has been demonstrated experimentally by others that distention of the biliary ducts caused marked distress, disturbance in respiratory rhythm, salivation, and often vomiting. The symptoms produced were generally more marked with distention of the ducts than the gallbladder. Section of the right splanchnic nerve was found often to abolish the distress and reduce the amount of the respiratory inhibition. Section of both vagi and the left splanchnic nerve stopped the salivation and vomiting and reduced the amount of respiratory inhibition, while section of both vagi and both splanchnic nerves abolished all distress and reflex disturbances.

Reference has previously been made to the studies on a series of conscious patients made by Zollinger on the effects of distention of the gallbladder and bile ducts. Distention of the gallbladder was found to cause moderate

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discomfort, no vomiting, and no referred pain. Distention of the cystic or common bile duct caused severe epigastric distress, vomiting in two of three cases, and no referred pain. He considered this evidence in agreement with Morley<sup>30</sup> that a true visceral pain does exist which is mediated through the sympathetics, and that inflammation of the peritoneum causes referred pain over a peritoneocutaneous reflex. Kulenkampff, as reported by de Takats, emphasizes the fact that muscular rigidity will disappear with splanchnic anesthesia in colic if it is of reflex origin. However, if rigidity is due to peritoneal involvement resulting from the contiguous extension of the inflammation or to adhesions, the rigidity will not be influenced.

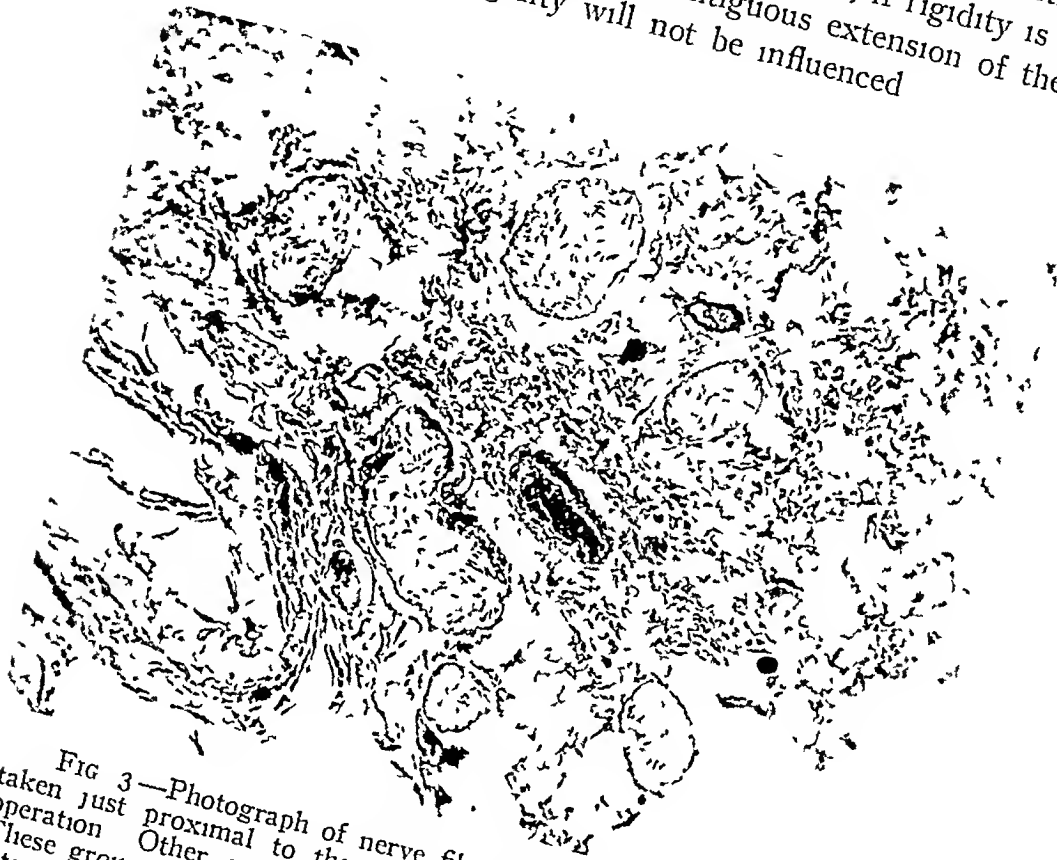


FIG 3—Photograph of nerve fibers in section of the cystic duct taken just proximal to the point where the duct was clamped at operation. Other nerve fibers were present in each cross-section. These groups of fibers in each case possibly represent the medial or lateral nerves of the gallbladder after branching has taken place.

From the above observations, it seems logical to assume that stimulation of the sympathetic nerves in the portal area would cause epigastric pain and some disturbance in the respiratory rhythm, while stimulation of the vagus fibers in the same area would cause dyspepsia and in some cases vomiting.

In an effort to determine whether an appreciable amount of nerve fibers were cut during the average cholecystectomy, a consecutive series of gallbladders sent to the surgical pathology laboratory from Barnes Hospital were sectioned transversely through the cystic duct just proximal to the point where the clamp had been placed. Figure 3 shows nerve fibers which were found in this area. The nerve trunks can be seen to be quite small and numerous as

branching of the larger trunks has occurred. Many other fibers on the other surfaces of the cystic duct are not shown.

Figure 4 is a gross dissection of a fresh anatomic specimen. The duodenum and pancreas have been rotated 90 degrees for clarity. The trunks from the celiac plexus can be seen passing to the hepatic plexus, probably the posterior portion which is in close proximity to the cystic duct and cystic artery. The medial branches are probably connecting branches passing to the anterior hepatic plexus along the hepatic artery. The lateral nerve of the gallbladder can be seen very clearly as it has been dissected free throughout



FIG 4—Dissection of adult specimen. The duodenum and attached pancreas have been rotated 90° to the left for clarity. A hook has been placed beneath three large nerve trunks which are passing superiorly from the region of the celiac plexus along the posterior and lateral surfaces of the common duct. The lateral nerve of the gallbladder can be seen distinctly with a hook near its termination. The posterior hepatic plexus can be seen just inferior to the cystic duct which has been retracted superiorly by the left black suture. The right black suture is around the cystic artery, and the right hook is attached to the medial wall of the hepatic duct.

its course along the cystic duct. It must be remembered that in the dissections and most of the illustrations, in the interest of clarity the structures in the portal area have been spread, whereas in reality they lie in relatively close proximity.

#### CASE REPORTS

Case 1—J. W., a white female, age 66, was first admitted to the Barnes Hospital, March 9, 1945, with a history that 11 years previously a cholecystectomy had been performed following episodes of right upper quadrant pain, with nausea and vomiting,

but with no chills or fever. Roentgenograms at that time showed stones in the gallbladder. At operation, one large and several small stones were found. She was asymptomatic for two years after operation. She then began to note a beginning return of some of the same symptoms for which she was operated upon the first time. These attacks at first lasted for about five minutes, and occurred every three or four months. There was no jaundice or alcoholic stools or dark urine. The attacks increased gradually in frequency and intensity during the intervening years. Pain in the right upper quadrant radiated down the subcostal ridge but not to the scapula or shoulder. There were no chills or fever but occasional nausea and vomiting. There was no jaundice. During the past few months she had had nearly daily attacks for which hypodermics had been ordered. The attacks were characterized by a cramping, colicky, right upper quadrant pain associated with

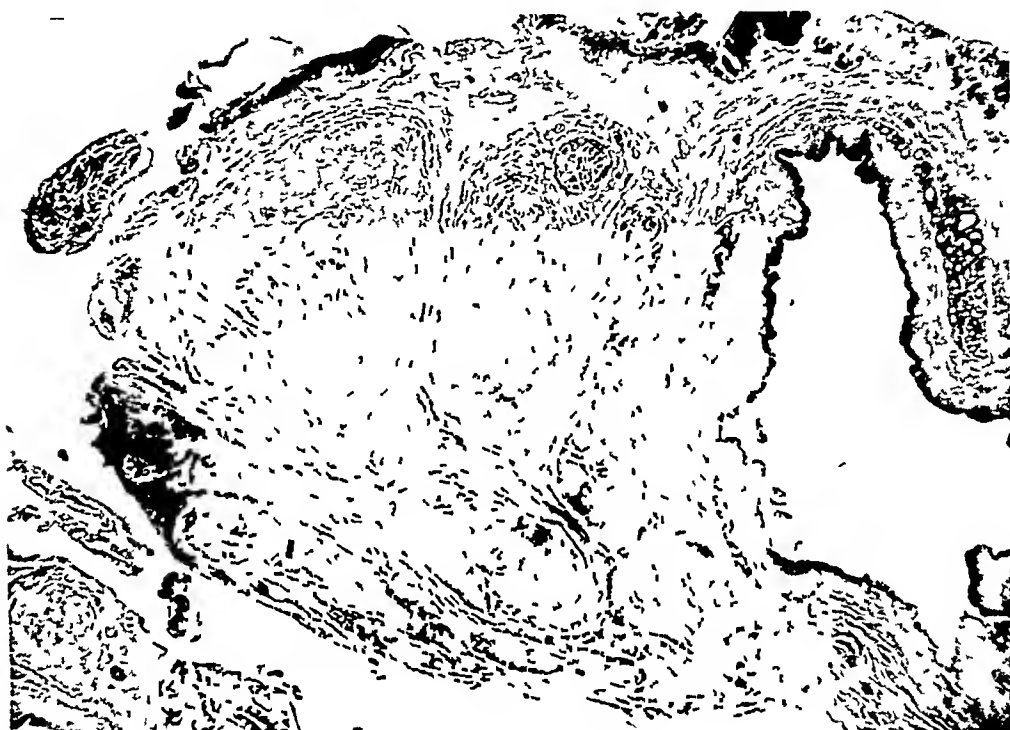


FIG 5—Case 1. Fibrous tissue overgrowth in regenerating nerves around the remnant of the cystic duct producing the picture of an amputation neuroma.

nausea and vomiting. More recently there was moderate jaundice, dark urine, and light stools, with some itching. In intervals between the attacks which were sudden in onset, the patient was asymptomatic.

Physical examination upon admission to the hospital was essentially within normal limits. The laboratory findings showed the urine, red and white blood cell studies, and hemoglobin to be normal. The nonprotein nitrogen was 19 mg per cent, fasting blood sugar 80 mg per cent, total plasma protein 6.3, with albumin of 3.7, and globulin of 2.6. Blood amylase was 143 units, and the icterus index was 7.5. The gastro-intestinal roentgenologic examination was normal, and the electrocardiogram was normal.

On March 15, 1945, the upper right rectus scar was excised by Doctor Womack, and very little musculature encountered. The omentum and duodenum were intimately adherent to the abdominal wall. They were dissected free with great care. The pelvic viscera were normal, as was the large bowel, with the exception of the appendix which was acutely kinked and dilated distally. This was removed and the stump inverted. The duodenum was now separated from the liver by sharp dissection and mobilized with the head of the pancreas, away from the posterior wall. The gastroduodenal artery, the

portal vein, the common bile duct, and the vena cava were identified. The common bile duct was enlarged two times, the wall was thin and colored a slate-blue. It contained no stones. It was separated from all fibrous tissue from the upper margin of the pancreas to the liver. The cystic duct had its origin from the mesial surface of the common duct, extending around posteriorly for a distance of 15 cm. It was enlarged to the size of one's little finger and had a bulbous tip. There were no stones present either in the cystic duct or common duct. The common duct emptied well, and was not explored. There were numerous large nerve trunks running into the stump of the cystic duct and the impression was that the patient's symptoms could be explained on the basis of an amputation neuroma. The cystic duct was cut-off close to the common duct and ligated with a silk suture. A drain was inserted to this area and brought out through a stab wound. The peritoneum was closed with No. 00 chromic catgut and the fascia brought together with interrupted silk, as was the skin.

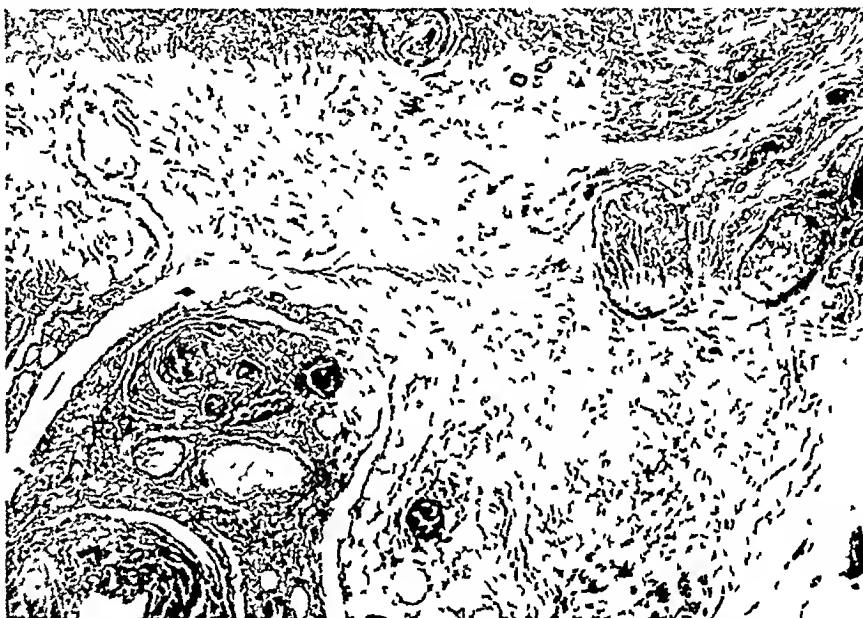


FIG 6—Case 2. Section taken through the remnant of the cystic duct near a fragment of the old chromic catgut ligature. Note the large nerve bundles and others such as seen in the lower right portion of the section, that are fragmented by scar formation.

The postoperative convalescence was uneventful.

Microscopic study of the portion of the cystic duct that was removed, showed a tremendous number of nerve fibers and trunks which were being invaded by an overgrowth of fibroblastic tissue, giving the classical picture of an amputation neuroma.

**Case 2**—A T, a white female, age 40, was first admitted into the Barnes Hospital, June 11, 1936, with a history that five years previously she had had sudden attacks of nausea followed by pain in the epigastrium which radiated to the midback. Jaundice later developed. This pain was relieved only by hypodermic injection. This was diagnosed as cholecystitis and a cholecystectomy was performed. Stones were said to have been found in the gallbladder at operation. She remained in the hospital for two weeks. Two days after returning home, she had a similar attack. Gastro-intestinal roentgenologic examination was then performed, but nothing abnormal was found.

Three years later she underwent a second operation in the same hospital, which supposedly was performed for adhesions which had been identified on roentgenologic

examination She again was in the hospital for two weeks There were no attacks after her second operation for six weeks Since then she had several attacks of pain in the epigastric region radiating to the back, associated with jaundice, fever, and clay-colored stools Diet seemed to have no influence on the onset of these attacks Since January, 1936, she had been having her stomach pumped every two weeks The stomach contents were always bile-stained

Physical examination upon her admission into the Barnes Hospital was within normal limits The red blood count was normal, as was the white blood count and differential Duodenal drainage was carried out and bile identified Blood amylase was 93 units

She was operated upon, June 20, 1936, by Doctor Heinbecker The abdomen was opened through an upper right rectus incision and the stomach was found adherent to the old gallbladder site There were numerous adhesions between the duodenum and the under surface of the liver General exploration of the abdomen revealed no abnormalities The stomach and duodenum were freed from the liver bed and the common bile duct exposed It was found to be of normal size Palpation did not reveal any stones The pancreas was soft, apparently normal The stump of the gallbladder, about one inch in length, had been left at the previous operation This was removed from below upward The cystic duct was small It was tied off close to the common duct There were no stones in this gallbladder remnant but its walls were thickened and the stomach and duodenum had been adherent to it The abdomen was closed in layers

Convalescence was uneventful, and she was discharged on July 6, 1936 Three months later a letter from the patient showed that there was not a great deal of improvement However, a letter five months later from the patient's physician said that she showed marked improvement The patient wrote two years later that she was now free from all symptoms, had gained 35 pounds, and was stronger than she had been in years

Microscopic examination showed the cystic duct to be involved in a considerable amount of fibrous tissue, running through which were a large number of nerve trunks, many of which were splitting up into smaller groups, such as is seen in amputation neuroma Surrounding the base of the whole mass was a small area of chronic catgut, which apparently had been present since the original operation This ligature had apparently grouped all of the adjacent nerve fibers together in one mass of scar tissue

Case 3—Mrs A M, a white married woman, age 55, was first admitted to the Barnes Hospital on April 2, 1945 She complained of epigastric pain and severe vomiting For some 10 or 15 years she had had intermittent epigastric pain coming on several hours after meals, which was relieved by taking food or milk These episodes were more frequent in the Spring and Fall There was not much change in these symptoms until November, 1944, when she began to vomit Because at one time she vomited a small amount of blood, her physician suspected a peptic ulcer She was also thought to have gallbladder disease As a result she was operated upon on December 6, 1944 A local physician told her that adhesions prevented the gallbladder from being entirely removed but that several stones were obtained Whether or not a partial cholecystectomy was performed we were never able to find out from the patient's record Following operation she continued to vomit for several weeks and required intravenous fluids During the past two weeks before admission she was unable to retain food in her stomach and had had intermittent epigastric pain and tenderness This patient presented a complicated picture of obvious cholecystitis and a duodenal ulcer

At operation, April 24, 1945, performed by Dr Gordon Moore, the common bile duct was identified and seemed to be normal except for slight dilatation The gallbladder remnant was extremely small, being only  $2.5 \times 1$  cm in diameter With considerable difficulty the cystic artery and cystic duct were identified The tiny gallbladder bed was reperitonealized It apparently represented only a small portion of the original viscus The

common bile duct was opened and a probe inserted easily into the duodenum and into the two hepatic ducts, without evidence of obstruction. A T-tube was sewed in place. A duodenal ulcer was present but it was felt wise to delay further surgery.

The patient made an uneventful convalescence, and was completely relieved of all of her epigastric pain. She returned at a subsequent date for gastric resection, which was undertaken for the duodenal ulcer.

Since her discharge there has been no recurrence of the biliary colic.

Microscopic examination of the excised remnant of cystic duct showed marked thickening of the wall by virtue of fibrous tissue, and in this scar tissue was embedded numerous large nerve trunks, some of which were being split, such as is generally seen in an amputation neuroma in which the fibroblastic proliferation invades the nerve trunks.



FIG 7—Case 3 Large nerve trunks involved in scar in a fragment of the wall of a cystic duct remnant

**Case 4—J S**, a 58-year-old married male, presented a history as follows. In 1941 he had had a cholecystectomy, with the removal of the gallbladder and stones. There had been preceding symptoms of biliary colic and dyspepsia for some 20 years. For one year after the cholecystectomy the patient had no symptoms. During the following two years he had four or five very severe attacks of right upper quadrant colicky pain which was referred to the right scapular region, which he describes as being typical in every respect to the colic he had had before his operation. These attacks of pain were not associated with chills, fever or jaundice.

During the recent months the pain has been less severe but the attacks more frequent. There has been very little dyspepsia between attacks and there is usually no nausea or vomiting during the attacks. He is able to eat almost any type of food. Physical examination showed a slightly obese male, with a large left indirect inguinal hernia, and an upper right rectus scar from the previous cholecystectomy. Blood pressure 140/94. The urine and blood cell studies were normal. The nonprotein nitrogen was 15 mg per cent, fasting blood sugar 65 mg per cent, icterus index was 10, urine contained no bile. Total plasma protein was 7.1, with albumin 4.3, globulin 2.8, and the blood amylase

determination was 86 units Cholecystography showed no visualization of the biliary apparatus Electrocardiogram was within normal limits, cephalin flocculation tests 1 plus, the stool negative for blood and positive for bile

The patient was admitted to the Barnes Hospital on February 10, 1946, and on February 14th, through an upper right rectus incision, removing the previous scar, the abdomen was explored Considerable scarring was encountered in the peritoneal cavity and the dissection was made slowly The duodenum was adherent to the under surface of the liver and was separated by sharp dissection The head of the pancreas was identified and found to be relatively uninvolved by scar The duodenum was mobilized and the common duct isolated This was found to be slightly enlarged above the level of the origin of the cystic duct and somewhat smaller below this level At the region of the origin of the cystic duct, there was a tendency toward hour-glass contraction, this being due to a nodular mass on the upper lateral surface of the common duct The duct



FIG 8—Case 4 Nerve trunks in a hard mass of scar overlying the common bile duct This tissue would be placed on tension with dilatation of the duct

was entered and explored No evidence of stones was found The nodular mass was dissected off the common bile duct with a remnant of the cystic duct The cystic artery was ligated separately The lesion appeared grossly as an amputation neuroma of the nerves to the gallbladder A T-tube was inserted and the defect closed over the T-tube in such a way that no narrowing of any considerable degree of the common duct was left The tube was brought out through a stab wound and the abdomen closed in layers with figure-of-8 No 30 steel wire

The postoperative convalescence was uneventful and before his discharge cholangiograms were done, showing the common bile duct to be normal The T-tube was left in place until 10-17-46, when the patient was readmitted into the hospital and the tube removed During this interval the patient had had no attacks of pain or any of the previous symptoms for which the procedure was carried out, although the tube had been kept closed for some time One month later the patient was still in excellent physical condition



## WOMACK AND CRIDER

Microscopic examination showed the most important lesion to be the nodular mass previously described, intimately adherent to the common bile duct. This mass was composed of a conglomerate of nerve fibers involved in scar tissue and placed in such a position that any change in diameter of the common bile duct would produce stretching of these scarred fibers.

Case 5—M. T., a 55-year-old farmer, was first admitted to the Barnes Hospital, February 5, 1945, at which time he gave a history of attacks of jaundice, right upper quadrant pain, vomiting, and fever which began about 1925. These symptoms became progressively worse so that he entered a hospital in a nearby city in 1942, at which time a cholecystectomy for stones was performed and the common bile duct explored. The gallbladder was subacutely inflamed and the common bile duct contained muddy material



FIG 9—Case 5 Nerve trunks in scar tissue that was stripped from the anterior wall of the common bile duct

The gallbladder was removed and a T-tube was left in place in the common bile duct. It was removed ten weeks postoperatively. Cholangiograms, taken at that time, showed what was said to have been a slight stenosis of the common bile duct. Following removal of the T-tube the patient's symptoms reappeared, with the exception that jaundice was questionable. He was readmitted to the same hospital, but no therapeutic procedures were recommended. He was unable to return to work and had not done so since the operation. He has numerous other complaints such as diarrhea, fatigability and dizzy spells. He had lost 25 pounds of weight during the preceding two months.

Physical examination showed a slight emphysema, heart sounds were faint, there was a healed abdominal operative scar, the prostate was symmetrically enlarged, the peripheral blood vessels were thickened, there was a fine tremor of the extended hands. Laboratory data showed the blood studies to be normal. The urine, stool, Kahn, icterus index, prothrombin time, blood sugar, blood nonprotein nitrogen, gastric analysis, spinal fluid, blood amylase, plasma protein, cephalin flocculation, and red blood cell fragility were normal. Four-hour glucose tolerance test was normal. Oral hippuric acid test showed a 69 per cent excretion. Stool examination showed no evidence of parasites, and allergy

## SYMPTOMS FOLLOWING CHOLECYSTECTOMY

skin tests were essentially negative. The gastro-intestinal roentgenologic examination showed a questionable deformity in the prepyloric region, with diverticulosis of the sigmoid. Electrocardiogram showed bundle-branch block.

He was discharged from the Barnes Hospital, February 15, 1945, and was readmitted on April 9, 1946, with a story that his symptoms had not been improved by medical care and that he was still completely disabled. He was operated upon by Doctor Womack on April 17, 1946. The old scar in the upper right rectus region was excised and in many areas the peritoneum was found adherent to the skin. The peritoneal cavity was entered and the liver identified. The stomach was adherent to the liver, the pyloric region and antrum being brought upward at an acute angle which probably accounted for some of the deformities seen in the roentgenologic examination. These adhesions were separated, the duodenum isolated and mobilized by sectioning the lateral peritoneum. The old gallbladder bed was freed and the common bile duct isolated. It was approximately 2 cm in diameter and thickened by several bands of dense fibrous tissue running across it in the region of the cystic duct. Because these bands might contain nerve fibers, they were dissected free from the wall of the common duct leaving the latter viscus a thin, bluish color when the dissection was complete. The duct was then opened and a lead probe passed through toward the duodenum. There was questionable resistance noted at the ampulla. A smaller probe was inserted and entered the duodenum easily. In order to establish the presence or absence of ampullary obstruction, an incision was made in the duodenum in the region of the ampulla. No obstruction was found. A diverticulum to the left of the ampulla, 1 cm in diameter and 1 cm deep, was identified, extending into the head of the pancreas. There was no ulceration about the diverticulum and no evidence of inflammation. A large probe was inserted through the common duct into the duodenum in order not to encroach upon the orifice, and the fundus of the diverticulum seized with clamps and inverted. The neck was ligated with a heavy silk suture. The duodenum was then closed. A T-tube was inserted into the common bile duct and the duct closed with interrupted silk. This tube was brought out through the abdominal wall by means of a stab wound and another small Carrel tube was placed along side it. The spleen was normal except for adhesions. The remainder of the gastro-intestinal tract was normal except the appendix which was long and contained two fecaliths. This was removed. The wound was closed with interrupted figure-of-8 sutures of No. 30 steel wire.

Since operation the patient has been free from his previous symptoms. The tube was removed one week after operation.

Microscopic examination showed that the heavy, fibrous tissue which overlay the anterior portion of the common bile duct and which was adherent to the peritoneum, consisted chiefly of large nerve trunks, through which bundles of collagenous fibrous tissue coursed. The position of this scarred nerve tissue was such as to be stretched whenever there was any dilatation of the common bile duct.

**Case 6**—G. T., a 33-year-old married colored woman, was first admitted into the Barnes Hospital, July 17, 1945, with a history of vague right upper quadrant distress, with gaseous distention, nausea and vomiting since she was age 16. These attacks were never very severe and sometimes would not occur for as much as a year. The symptoms never lasted more than a day.

In June, 1943, at another hospital, she had been operated upon for gallbladder disease. At this time her common bile duct was obviously injured as the patient began to discharge bile immediately through her wound and later became jaundiced. Subsequently, she was re-explored but nothing apparently was done. At this time she began to have fairly severe attacks of upper right quadrant pain similar to biliary colic in every respect, much more pronounced than before her original operation. She was also deeply jaundiced, and there was no discharge of bile through her incision when we first saw her.

She was operated upon at the Barnes Hospital, July 27, 1945, at which time she

exhibited severe liver damage. The portal vein was identified, and a dense fibrous structure seen and felt which must have been the obliterated common bile duct. The distal part seemed hard and indurated and a small portion of the surrounding scar was removed for biopsy. After careful dissection, a gray, turbid bile was obtained from a point which proved to be a dilated common duct at the surface of the liver. This was opened and a fairly large amount of the same white bile, with inspissated mucus and other material escaped. This area proved to be the junction of the right and left hepatic ducts. In view of the poor condition of the patient and the marked liver insufficiency, a tube was inserted for temporary external biliary drainage until the function of the liver improved considerably. Anastomosis was to be performed at a second stage.

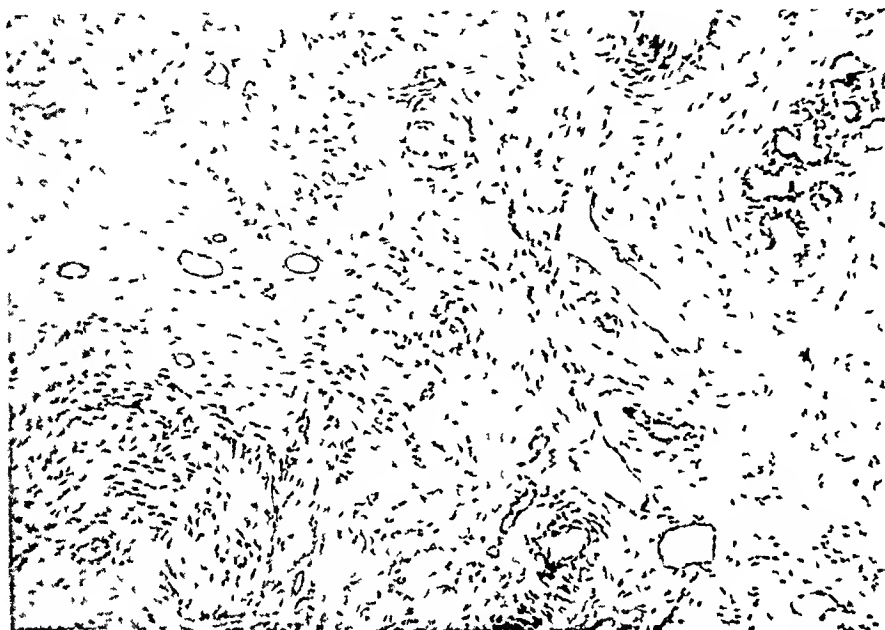


FIG 10—Case 6. Large and small nerve trunks adjacent to the dilated portion of a strictured common bile duct. This patient developed biliary colic after the formation of such scar. The colic was relieved after excision of the scar.

Unfortunately, her jaundice never disappeared. The secretion of bile became less and finally ceased completely. Another exploration showed the biliary obstruction to now be intrahepatic.

Microscopic examination of the tissue removed at operation from alongside the common bile duct shows large and small bundles of nerve fibers completely enmeshed in dense, fibrous tissue, producing a picture similar to that described in previous cases.

**COMMENT** In the consideration of the anatomic and pathologic findings described in the preceding pages, there are certain aspects worthy of further comment. It is to be particularly noted that the size of the nerve bundles and the number of the nerve fibers distributed along the common bile duct and the cystic duct are sufficient to be of clinical significance. As has been pointed out, there is now sufficient clinical and experimental evidence obtained from observations on both animals and the human to demonstrate that stimulation

of these nerves results in symptoms identical to those experienced in biliary tract disease

We have called attention to various types of lesions seen involving these nerve fibers in our experience with patients who have a persistence of their symptoms of biliary tract disease following cholecystectomy. As has been stated, attention has previously been called to the relationship of the persistence of a large cystic duct to the presence of such symptoms. We have also found this to be one of the common findings at operation. However, it is our feeling that it is not the persistence of a large cystic duct *per se* that produces disability, but rather the inclusion in the scarred walls of that duct of bundles of nerve fibers, chiefly sympathetic in type, with perhaps a smaller number of vagal fibers. At times, fibrous tissue proliferation and nerve trunk regeneration may result in a nodularity resembling the classical form of amputation neuroma. It will be recalled from the anatomic description of the distribution of these fibers, that both the anterior and posterior plexus tend to converge in the region of the cystic duct so that it is sometimes quite easy to include many of these fibers in the ligature about the cystic duct. At such a time there may not be true neuroma formation, but rather a constriction and ischemia of the nerve fibers in a region that is subject to variation in intraductal tensions during the day.

Another type of lesion noted in the nerve plexus has to do with the laying down of a diffuse sheath of dense fibrous tissue over the anterior surface of the common bile duct in the region of the stump of the cystic duct. Because of fear of injury to the common bile duct, this fibrous tissue is often not studied adequately. When it is removed and microscopic section made of it, in our experience it almost universally shows the same type of nerve trunks enmeshed in scar tissue as has been described above.

One of the most interesting observations in our experience has to do with that demonstrated in Case 6. Here was a thin young girl giving a clinical history that was not particularly suggestive of gallbladder disease, and certainly before her operation she had never complained of pain resembling that seen in biliary colic. Following the removal of what could easily have been a normal gallbladder, with subsequent damage to the common bile duct, there was sufficient scarring of the nerve supply to the common bile duct to result in a classical picture of biliary colic.

The presence of scar tissue around nerve trunks produces both stretching of the fibers and ischemia. Both of these factors, as has been well-demonstrated, lower the threshold of stimulation of nerve endings and nerve trunks. The presence of the damage, therefore, that has been described, is such as to make those nerve fibers present much more susceptible to stimulation, and what in a normal environment would be a stimulus so mild as to be clinically imperceptible, could now become one with considerable exaggeration. It would seem to us that the position of these damaged fibers about the expanding and contracting common bile duct and occasionally the cystic duct, is adequate to explain the origin of this stimulus.

Another interesting feature about this study has been the time element. As a general rule, several months usually elapse after the cholecystectomy before the recurrence of symptoms begins to appear. This would be in keeping with the laying down of the dense collagenous scar. Furthermore, we are familiar with many instances in which these postcholecystectomy symptoms have appeared and after a few years disappeared. This we would interpret as being due to complete degeneration of the damaged nerve trunks.

In order to prevent the appearance at a later date of such symptoms as have been described, it has been our practice for some time now, wherever possible, to separate the nerve trunks mesial to the common bile duct. In most instances, this is fairly easily done if the peritoneum and underlying areolar tissue is removed from over the common bile duct before the gallbladder is resected. The nerve trunks can then be well-visualized and lifted up with a blunt clamp and sectioned. At the same time, the common bile duct is cleaned of all surrounding areolar and fibrous tissue. Occasionally, a situation develops in which such treatment of the common bile duct would be fraught with considerable danger. At such times, it has been our experience that the best treatment has to do with stripping completely the cystic duct of all of its adjacent structures as well as the cystic artery. In this way none of the nerve fibers are caught in the ligature.

In those patients that have been operated upon for the so-called postcholecystectomy syndrome, a similar plan of procedure is carried out. At this time, whenever present, the stump of the cystic duct is removed close to the common bile duct. Any scarring present on the surface of the common bile duct is carefully removed. The nerve trunks, as a rule, become well-visualized on the mesial side of the common bile duct and can likewise be destroyed at that time.

#### SUMMARY

1 From 5 to 20 per cent of patients with characteristic symptoms of cholecystitis, and with the classic pathologic findings at operation, will continue to have their symptoms in varying degrees of severity following cholecystectomy.

2 Considerations previously advanced as to the cause of the persistence of these symptoms have been discussed.

3 The nature of the nerve supply to the bile passages is described, and pathologic lesions seen in these nerve pathways in patients with persistent symptoms following cholecystectomy are demonstrated.

4 Effective prevention and treatment is outlined.

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# BEZOARS CAUSING ACUTE INTESTINAL OBSTRUCTION\*

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A BEZOAR is currently described as a concretion usually found in the stomach or intestines of certain ruminates and is composed of various vegetable matters, hair, *etc*. The composition of the bezoar determines its class, namely, trichobezoar composed mostly of hair, phytobezoar composed of vegetable matter, and (3) trichophytobezoar, a combination of these two.

In the 58 years of this association there has been only one paper presented before it dealing with the subject of bezoars. This was presented in a most interesting and instructive paper by Dr. Rudolph Matas,<sup>1</sup> in 1914. This presentation dealt exclusively with the trichobezoar, or hair balls, in the stomach, special attention being directed toward the preoperative diagnosis of this condition by means of the contrast media and roentgenograms. At the time of this paper there were 73 reported cases in the literature to which the author added one of his own. In the "Supplementary Commentaries on Bezoars" at the end of this article Doctor Matas writes in his own inimitable way concerning the history of bezoars and the important part they played in the "pharmacopeia of antiquity and of the middle ages, even up to the eighteenth century."

We have said that this subject has been presented only once before this association, at the same time it should be noted that the most exhaustive and recent study of the subject is by two members of this association, Dr. Alton Ochsner and Dr. Michael DeBakey<sup>2,3</sup>. This study comprises a thorough search of the world literature up to 1938, at which time there were 171 cases of trichobezoars, 119 cases of phytobezoars and 13 cases of other concretions. This plus their seven additional cases comprised a total of 126 phytobezoars and because of the fact that 92, or 73 per cent, of these bezoars were due to the ingestion of persimmons they suggested the term "diospyrobezoar" from the Greek *diospyron*, translated as "Jove's grain," the generic term for the wild persimmon.

\* The most recent report on the bezoars that we have been able to find in the literature is by Miller and Keit,<sup>4</sup> on "Trichobezoar," from the Journal of the Mt. Sinai Hospital, April, 1944. These writers report three cases occurring in Mt. Sinai Hospital, two being intragastric, while the third suffered from combined gastric and multiple intestinal trichobezoars. This last patient died, whereas the other two recovered.

It is to be noted that in the eight cases of bezoars reported by DeBakey and Ochsner only one was composed of hair and seven were composed of

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\* Read before the 58th Annual Session of the Southern Surgical Association, Hot Springs, Va., December 12, 1946.

vegetable matter, mostly the wild persimmon, whereas in three cases reported from Mt Sinai Hospital all were composed of hair. This difference is no doubt accounted for by the geographic difference between New Orleans, in the South, where the wild persimmon flourishes and New York, in the East, where this fruit grows sparsely, if at all

While the composition of bezoars can be easily determined and the reason for the ingestion of the vegetable matter causing most phytobezoars is easily understood, the reason or reasons for trichophagia remains a mystery. In cases of trichobezoars where sex was noted 139 were female and 13 were male. This would suggest that the long hair of the female is certainly one of the underlying causes. However, "when the incidence was listed by decades and the long or short hair style of the decade is noted, no significant variation is apparent."

In the case of phytobezoars the records show about 3 to 1 in favor of the male.

Trichobezoars are found most frequently between the ages of 10 and 19, whereas the phytobezoars are found most frequently between the ages of 50 and 59.

Throughout the literature the emphasis is placed on the diagnosis and treatment of gastric bezoars. In some reports mention is made of the fact that portions of the trichobezoars may break off, producing intestinal obstruction, and the operator is cautioned about examining the bowels for these cast-offs when removing one from the stomach. However, very few cases of obstruction have been reported. In discussing Doctor Matas' paper Dr. Le-Grand Guerry mentioned a case in his practice of acute intestinal obstruction caused by one of these.

In Matas' report six of 44 operated cases had hair balls in the intestines but none of these seem to have caused acute obstruction.

DeBakey and Ochsner also mention the "possibility of such complications as intestinal and gastroduodenal ulceration, with consequent hemorrhage, perforation and peritonitis."

While the diagnosis of intragastric bezoars, especially trichobezoar, may often be made preoperatively the same is not true once the bezoar has passed into the intestinal tract and produced obstruction. The case then presents the usual picture of acute intestinal obstruction, the cause of which may only be suspected if there is a suggestive history. In the eight cases reported by DeBakey and Ochsner there were three cases of intestinal obstruction caused by phytobezoars of persimmon origin. A definite history of having eaten persimmons prior to the onset of illness was obtained in two of the three cases, in one case only a few days before, whereas in the other 11 months had elapsed. In both cases the cause of the obstruction was predicted before operation.

Heffels<sup>5</sup> reports a case of high obstruction in a 56-year-old woman suffering from schizophrenia.



In the three cases that have come under our observation the bezoars were all found in the small bowel, causing acute obstruction. Two of these were phytobezoars and one a trichobezoar. We must admit that we failed to determine the etiologic factor before operation in any of the three cases, whereas it should have been suspected in two of the three. In Case 2 and 3 a history of having eaten persimmons and a history of trichophagia, respectively, were obtained following operation.

#### CASE REPORTS

**Case 1**—The first case is that of a white male, age 73, admitted to the hospital complaining of pains in the abdomen, nausea and vomiting.

*Present Illness*—The patient began having colicky pains in the abdomen four days before admission. Twenty-four hours later he became nauseated and vomited. The pain continued mostly in the right side and each day there was continued, but not frequent, nausea and vomiting. There had been no movement of the bowels.

*Physical Examination*—This revealed an elderly white man, age 73, in poor physical condition. The temperature on admission at 10 00 A.M. was 98° F, pulse 120, quite irregular. B.P. 110/90. The heart sounds were distant, feeble and irregular. The abdomen was distended, especially in the lower half, while the skin over the right lower quadrant was blistered from hot applications. No mass was palpable but there was definite tenderness over McBurney's point and below. *Laboratory Data*—These showed a normal urine. N.P.N. 35 mg. W.B.C. 13,500, polys 84 per cent. Hb 90 per cent. *Preoperative Diagnosis*—Acute intestinal obstruction of undetermined etiology.

*Treatment*—The patient's condition on admission would not permit immediate operation, but following saline infusions this improved to such an extent that operation under local anesthesia was undertaken eight hours later.

*Operation*—Under local anesthesia of 1 per cent novocaine, a low right rectus incision was made. A moderate amount of straw-colored peritoneal fluid was present. The appendix was normal. There was a moderate distention of the small bowel leading to a mass in the pelvis which, when pulled up into the wound, proved to be within the lumen of the lower ileum. The abdominal cavity was carefully packed-off with moist gauze packs and the mass removed through a two-inch incision in the free border of the bowel. The bowel was then closed with two layers of fine catgut and the abdominal wound in layers, without drainage.

*Pathologic Report*—"The specimen is a mass of greenish-black substance, measuring 5 x 3 x 2.5 cm, which when cut is found to be composed of dried vegetable fibers." There was nothing in this report to identify the specimen as of persimmon origin.

The convalescence in this case was rather stormy because of wound infection, but he was dismissed from the hospital on the 16th postoperative day, in good condition.

**Case 2**—The second case was that of a white male, age 60, admitted to the hospital, March 27, 1939, complaining of pain in the abdomen, nausea and vomiting.

*Present Illness*—For about one year the patient had complained of epigastric discomfort, especially following meals, and had been under treatment for supposed duodenal ulcer, although there had been no roentgenologic studies. The day prior to admission to the hospital he was seized with severe abdominal cramps, especially in the upper part, accompanied by severe nausea and vomiting.

*Physical Examination*—This showed the patient to be a well-developed man, age 60, apparently suffering acutely. Pulse 84, temperature 99.4° F, B.P. 146/82. Heart and lungs normal. Urine normal except for a trace of acetone and diacetic acid.

## BEZOAR OBSTRUCTION

Interest centered chiefly on the abdomen, but, even here, there was nothing very striking—only moderate distention in the upper half associated with a moderate amount of tenderness, no spasm and no palpable mass

In view of the uncertainty of the diagnosis roentgenologic examination was made with the following report "Fluoroscopic survey of the chest showed no pathology of heart or lungs Plain film of the abdomen showed no distended loops of bowel A barium meal was given The esophagus, stomach and duodenum were normal Five hours later examination showed a complete obstruction to the passage of barium at a point in the jejunum about 12 inches distal to the ligament of Treitz No barium passed this point A recheck two hours later showed no change" *Preoperative Diagnosis* Complete, high intestinal obstruction of unknown etiology

*Operation*—Through an upper right rectus incision the abdomen was opened, and the jejunum, containing a firm rounded mass, was delivered onto the abdomen The abdominal cavity was packed-off carefully with warm moist packs and intestinal clamps



FIG 1 —Trichobezoar which produced complete small bowel obstruction Removed from lower ileum

applied The bowel above the mass was moderately distended while that below was flat Through a longitudinal incision on the free surface of the bowel the mass was removed and the wound closed with three layers of suture The abdomen was closed in layers, without drainage

*Pathologic Report*—The pathologist described the specimen as a large mass roughly triangular in shape, measuring  $6 \times 4 \times 4$  cm through its thickest portion it was 4 cm It had a putrefactive, fecal odor and was covered by a dirty greenish-grey film When sectioned, the interior of the mass was brownish in color and in it were masses of vegetable and fruit peelings and many seeds

Postoperative questioning of the patient revealed that he had eaten heartily of persimmons, which grew plentifully on his farm

*End-Result* Complete, uneventful recovery

**Case 3**—The third case is that of a white female, age 5, presented by her mother, with the chief complaint of nausea, vomiting and abdominal pain

*Present Illness* For the past six months the child had been complaining of anorexia, and during the past three months with intermittent attacks of constipation, abdominal pain, nausea and vomiting On the day of admission these symptoms became more marked, and were associated with elevation of temperature and pulse

*Physical Examination* This revealed a rather thin, pale, white girl, age 5. Temperature  $100.4^{\circ}$  F. Pulse 120. Other physical findings were within normal limits except for generalized abdominal distention and tenderness without rigidity. There was some voluntary muscle spasm in the right lower quadrant but not enough to prevent palpation of an elongated mass, which was about the size of a man's thumb. This mass lay approximately midway between the umbilicus and right anterior superior spine, moderately sensitive to palpation, and slightly movable. No roentgenologic studies were made since the case was one for immediate surgery. *Blood count* WBC 14,000, polys 84 per cent. *Preoperative Diagnosis* 1. Acute appendicitis. 2. Intussusception.

Prior to operation foreign body was not even considered in this case. An acutely inflamed appendix wrapped in omentum may give a similar picture. Intussusception was considered as a possibility because of the movable, elongated mass, although there had not been any blood in the stools and the child was above the age when this usually occurs.

*Operation* This was done through an extended McBurney incision. There was an excessive amount of straw-colored peritoneal fluid, and immediately beneath the incision appeared a large, elongated firm mass within the lower ileum. The loop of bowel containing the mass was easily delivered onto the abdominal wall, the abdominal cavity was



FIG 2—Same as Fig 1. Note constriction, probably caused by pyloric muscle before final expulsion from the stomach.

carefully packed-off with warm moist gauze and a two-inch longitudinal incision was made along the free border of the bowel exposing and delivering a foul-smelling mass of matted hair, measuring  $9 \times 3 \times 3$  cm, and retaining roughly the contour of the stomach (Figs 1 and 2). The bowel was closed with two layers of fine catgut suture, and the abdominal wound closed in layers, without drainage.

*Postoperative Diagnosis* Trichobezoar, causing complete obstruction. Recovery was uneventful and, as far as we have been able to determine from the mother, this experience has cured the child of eating hair. Following the operation the mother, when questioned, stated that she had never actually seen the child eating hair but had frequently noted loose hairs in the bed and bald spots on her scalp since infancy, but had never attached any significance to it.

In our search of the literature we have been unable to find a recorded case in which a trichobezoar has passed out intact through the pylorus into the lower bowel, resulting in obstruction, all the other acute intestinal obstructions from trichobezoars were caused by fragments that had broken off from a gastric bezoar and passed through the pylorus.

SUMMARY

- 1 A brief review of the literature on the bezoars is given
- 2 Two cases of phytobezoars and one of trichobezoar are added
- 3 All three cases were causing acute intestinal obstruction, were operated upon, and all recovered

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DISCUSSION —DR JOSEPH W COLLINS, Portsmouth, Va In 1938 I had the privilege of reporting a case of recurrent trichobezoar before this Association The patient was a young girl, age 7, who had a palpable tumor in her upper abdomen Her mother said that she had appeared to be a normal infant in all respects, but as soon as she started to crawl she began to pick up foreign bodies and swallow them These consisted of hair, strings, tacks, match sticks, pins and small pieces of glass, paper, chicken feathers and, in short, whatever she could put her hands on Her mother found many of these objects in her stools At the age of two she began to pull her own hair and swallow it This strange appetite continued and, at the age of five, she began to lose weight and complain of pain in her upper abdomen Her appetite for food was poor She had frequent attacks of nausea and vomiting These symptoms persisted until her admission to the hospital

Operation revealed a large hair ball completely filling her stomach There was a prolongation of it through the pylorus and duodenum into the jejunum for a distance of 13 inches The pyloric opening was greatly dilated, but no gross pathologic lesions were encountered This hair ball weighed one pound, eight ounces, and was S-shaped, forming a mold of the stomach, duodenum and part of the jejunum The mass consisted chiefly of hair, but many other foreign bodies were also evident

When this child reacted from her anesthetic she began to beg for food Her demands were so insistent and so noisy that it was necessary, for the comfort of other patients, to keep her completely narcotized until mouth feeding could be safely resumed She made an uneventful recovery

Eight years later she was again admitted to the hospital because of pain in the upper abdomen She was now a girl of 15, and had been attending high school until she was forced to leave school because of her illness The pain in the abdomen was more or less constant, but at times it became a severe colic These symptoms began about four months before admission Her condition had grown steadily worse since onset of symptoms, and her weight had dropped from 128 pounds in September, 1934, to 99 pounds upon admission In the light of her history and physical examination it was plainly evident that she had accumulated another hair ball Roentgenologic examination, after administration of barium meal, showed the stomach to be completely filled with a solid mass Her abdomen was again opened and a large, twisted, S-shaped hair ball was removed, this weighed one pound, two ounces, and completely filled the stomach and duodenum It

consisted almost entirely of black hair. In the first part of the jejunum, about seven inches from the duodenojejunal junction, three small hair balls could be palpated. One of these had a very sharp edge which had ulcerated through the wall of the intestine. This perforation was covered by the omentum. A portion of the proximal end of the jejunum and its mesentery was much indurated and inflamed, and there were numerous enlarged, inflamed mesenteric nodes in this region. With this extensive pathologic condition in the jejunum it was deemed advisable to resect the damaged portion rather than attempt to repair the perforation. Resection of the damaged segment and side-to-side anastomosis was therefore performed. The resected intestine contained the three small hair balls. Immediately distal to the inflamed portion of the jejunum there was an intussusception. This was apparently of recent origin and was easily reduced. The abdomen was closed without drainage, and again the patient made an uneventful recovery.

Upon reviewing the literature I found only three other cases reported in which there had been a recurrence. One of these was a woman who had had five hair balls removed.

DR. JAMES D. RIVES, New Orleans, La. If I may be permitted a certain amount of flexibility in the use of the term bezoar, I would like to report another of these curious cases. This was a white female child, six years of age. She was undernourished and somewhat mentally deficient. Roentgenologic examination showed the duodenum to be about the same size as the stomach, and to contain a number of assorted foreign bodies.

At operation, the duodenum was opened, and an heterogeneous accumulation of odds and ends was removed, it included leaves, paper, seeds of various kinds, buttons, and a coin. One ring, visualized roentgenologically, could not be found, and presumably was passed per rectum. At the time, I believed that the duodenal dilatation was due to this mass of foreign material, and thought its removal was sufficient. However, she returned after one year with an equally ill-assorted collection of material in the duodenum, and roentgenologic examination suggested the existence of duodeno-mesenteric ileus. It became apparent that since nothing could be done about her eating habits something must be done about the disposal of what she swallowed. At operation, a large amount of foreign material similar to that removed at the first procedure, was found and removed. A very large duodenojejunosomy was made.

This procedure seems to have been successful since, while she continues to swallow anything she can lay her hands on, all of it has so far passed through the intestinal tract.

DR. J. M. DONALD, Birmingham, Ala. Doctor Watt has presented to us a most interesting subject.

I would like to report a case of phytobezoar (persimmon ball) of the stomach, with a perforated gastric ulcer as a complication. This case has not been previously reported. I have been unable to find a similar case in the literature.

**Case Report**—This 27-year-old white male was admitted to the surgical service of the Hillman Hospital on February 9, 1936. He gave a history of having noticed epigastric pain for the past three weeks. The pain developed several hours after meals and was relieved by food. For the past two weeks tarry-colored stools were noticed. There was no history of previous attacks. Six days before admission he began to vomit dark brown material and the epigastric pain increased. Approximately 19 hours before coming to the hospital, and after taking a large dose of Epsom salts, he developed severe epigastric pain requiring morphine for relief. The picture on admission was that of acute perforation of a peptic ulcer, with peritonitis, and a respiratory infection.

Immediate exploration, under spinal anesthesia, revealed a generalized peritonitis due to a large perforation of a gastric ulcer situated on the anterior wall of the stomach in its middle third. A large, firm mass was palpated floating in the stomach contents. The stomach was opened and a large phytobezoar was removed. It weighed 3.5 ounces and measured  $10.5 \times 5.5 \times 4.5$  cm. It was stained black and had assumed the shape of the stomach. The defect in the stomach was closed in layers and the abdomen was closed, with drainage. While on the operating table the patient gave a history of having eaten a hat full of persimmons in one sitting, in the Fall preceding operation.

Death from peritonitis and bilateral lobar pneumonia occurred two days after operation

It was our opinion that the gastric ulcer was caused primarily by the mechanical irritation of the gastric mucosa by the persimmon ball

DR CHARLES H WATT, Thomasville, Ga, (closing) I want to thank you for this discussion and I also wish to apologize to Doctor Collins for having overlooked the report of his case I note he reported it before this Association in 1938

# SURGICAL CURE OF URINARY INCONTINENCE IN WOMEN\*

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INCONTINENCE OF URINE of varying degree in women is one of the common complaints heard in every gynecologic clinic. When the symptom is of a marked degree, there is nothing more distressing to the patient. Not only is there the physical discomfort associated with constant moisture and local irritation, but there is an unmistakable odor of decomposing urine which is annoying to the patient and those in proximity to her. The constant fear of visibly wetting her outer clothing is trying on her nerves and she may shun society and ultimately lead the life of a recluse.

To talk to these victims is to be convinced that no surgeon can do a more humane act than give them relief. Unfortunately, surgical results, in general, are not as satisfactory as they should be. The great numbers of women who seek relief at the larger clinics, after numerous previous unsuccessful operative attempts, amply support this statement. There are many reasons for these failures. One of the principal reasons is our lack of knowledge of the exact anatomy of the parts and our failure to know completely the physiology of micturition. Another is the lack of training in female urology of surgeons, gynecologists and obstetricians who attempt plastic operations to restore continence. The necessary skill to cystoscope, and thus examine the bladder and urethra from within, is a great advantage to the surgeon from a diagnostic and surgical point of view. Because the symptoms of incontinence are so distressing, the patient urges the doctor to cure her promptly. Since the surgeon or obstetrician often feels a sense of guilt in having had a hand in causing the condition, he may yield and operate too soon, before sufficient time has elapsed to get the tissues in condition for plastic surgery.

We have had rather extensive experience in urinary incontinence in the female at the Gynecological Clinic of the Johns Hopkins Hospital, where a division of female urology is an integral part of the clinic. It was thought that our experience of the past decade might be reviewed so that we can profit in the future from our mistakes and experiences in the past. This paper is concerned with such a review.

The types of incontinence considered in this series are briefly summarized below. It is conceded that there are other rare types, such as those due to extrophy of the bladder and ectopic ureters opening into the vagina or urethra, but they each require special consideration and are not included in this series.

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1 *Stress incontinence* of different degrees, varying from slight, occasional loss of control on severe straining at coughing, sneezing or lifting heavy weights to almost complete incontinence which occurs with the slightest exertion. Stress incontinence is usually associated with cysto-urethrocele, with or without uterine prolapse, but occasionally is seen without these conditions, and even in nulliparous (usually elderly) women.

2 *Vesicovaginal fistulae*, due to childbirth injuries, surgical injuries and destruction of the vaginal and bladder walls by malignant disease of the pelvic organs and/or irradiation therapy.

3 *Defects in the urethra and sphincters*, due to congenital defects, obstetrical and surgical accidents, or destruction by malignancy or lymphopathia venereum.

4 *Incontinence due to neurologic disease*, such as spina bifida, multiple sclerosis or tabes dorsalis.

5 *Ureterovaginal fistulae*, due to operative or irradiation injuries.

6 *Inflammatory lesions of the urinary tract*, causing such marked frequency and urgency as to result in practical incontinence. No cases of this type are included in this series because, strictly speaking, they should not be classified as incontinence and their treatment, obviously, is not surgical. However, it is extremely important that they be recognized and differentiated from those cases in which there is a defect in the sphincter mechanism or bladder or ureteral walls. A careful history will usually identify this group, but cystoscopic examination should often be done for confirmation.

#### STRESS INCONTINENCE

The causes and cure of stress incontinence will be considered first. It is many times more frequent than all of the other types combined. It is the simplest type to cure surgically and yet results are not uniformly satisfactory. Kelly and Dumm<sup>1</sup> reported 80 per cent successful, B. P. Watson<sup>2</sup> 65.7 per cent and H. Dawson Furniss<sup>3</sup> 76.5 per cent.

There is more than one etiologic factor in stress incontinence. This was recognized as early as 1913 by Kelly,<sup>4</sup> who noted that some cases occurred in association with cystocele and others occurred without any visible lesion. B. P. Watson found that two out of every three women with stress incontinence had cystocele, and our experience coincides with his.

The explanation for the incontinence in those cases associated with cysto-urethrocele or urethrocele lies in the sagging of the urethra and base of the bladder. It is the sagging of the urethra and the immediately adjacent trigone rather than the higher portion of the bladder which is the chief factor in loss of control. In many cases of cystocele and/or uterine prolapse when the urethra maintains its normal position snugly attached beneath the symphysis there is no incontinence. Defects in the pubovesicocervical fascia, which normally supports the urethra and bladder, are responsible for both urethrocele and cystocele. Coughing, sneezing and other physical exertion forces the unsupported undersurface of the urethra and bladder downward, while the



anterior surface remains in apposition to the symphysis. This prevents the urethral sphincter muscles from closing in a normal concentric manner and the resulting oval sphincter aperture fails to completely shut off the flow of urine (Fig 1). The gush of urine can be prevented in most of such cases by making slight pressure against the undersurface of the urethra when the patient coughs, thus, giving the urethra the support which it normally gets from the intact pubovesicocervical fascia.

The women without cysto-urethrocele usually present themselves after middle age, and the only explanation which can be offered is a decrease in

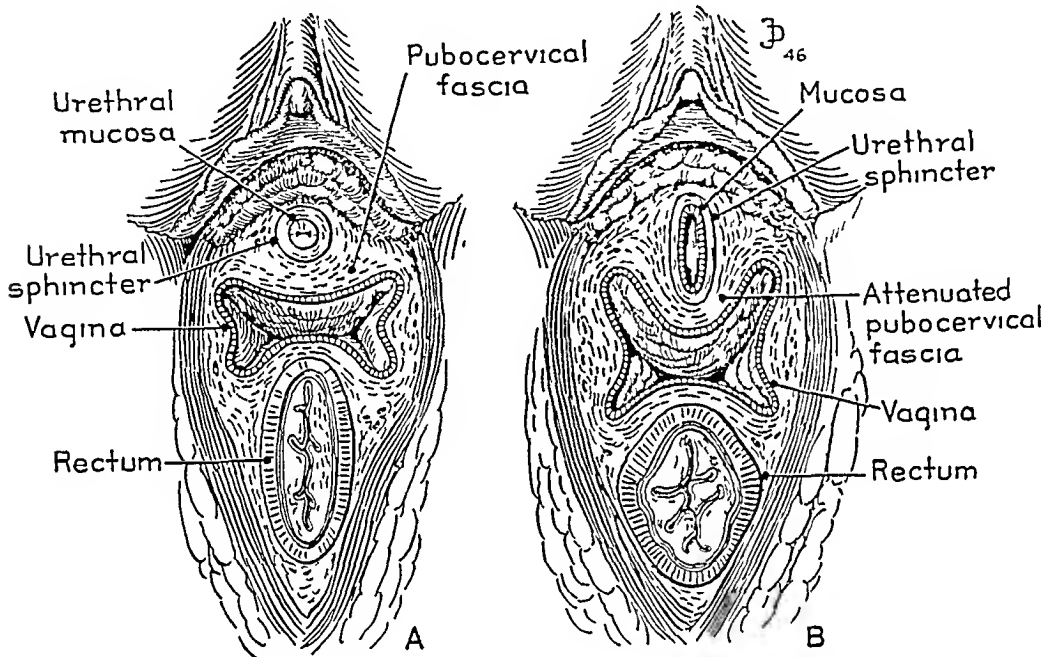


FIG 1—A Schematic representation of camera shutter-like action of normal urethral sphincter

B Schematic representation of failure of urethral sphincter to close on straining after development of urethrocele

sphincter muscle tone occurring with advancing years. However, it is difficult to prove this assumption, even by inspecting the urethral sphincters cystoscopically. The smaller percentage of cures obtained by sphincter plication in this group would seem to substantiate the view that the musculature is not up to par.

There is still another group of women who suffer from stress incontinence. These women may have had one or more vaginal deliveries or unsuccessful operations for stress incontinence. Indeed, the loss of control may follow operations for cysto-urethrocele in women who had no previous incontinence. The author has had two such instances in his practice, and Kennedy<sup>5</sup> has reported similar cases. The explanation lies in the formation of scar tissue in the periurethral region, preventing the camera shutter-like action of the sphincter.

muscles Visualization of an imperfect closure can, in some instances, be demonstrated cystoscopically Kennedy<sup>5</sup> has particularly stressed the importance of these periurethral adhesions and has devised an operation for the restoration of continence in such cases His operation will be discussed later

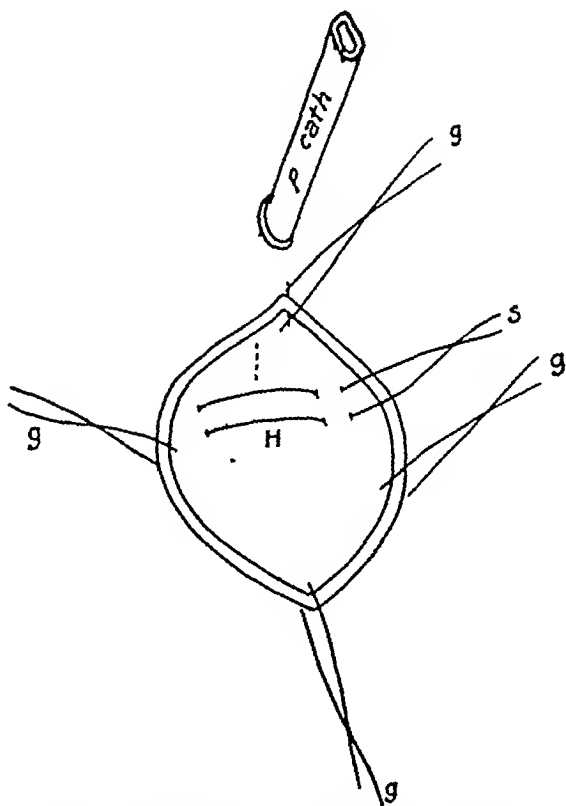
#### OPERATIVE PROCEDURES FOR CURE OF STRESS INCONTINENCE

The procedures for the cure of stress incontinence are the plication of the vesical sphincter musculature and reuniting the pubovesicocervical fascia fibers beneath the urethra and base of the bladder Plication of the vesical sphincter was probably first done by Howard Kelly, although all authors do not agree on this Schumann,<sup>6</sup> for example, states "The best procedure for this purpose in my experience is a modification of that proposed by Baldy, in 1913, and afterward described by Kelly, by whose name the operation is most generally known" This difference of opinion stimulated the author to investigate the records on the subject and the facts in the literature are as follows

In 1913, Baldy<sup>7</sup> reported on two patients with stress incontinence which he cured by denuding an oval of vaginal mucosa and the underlying fibrous tissue beneath the neck of the bladder and closing the wound with interrupted silkworm gut sutures In making this closure he picked up the denuded vesical neck with some of the interrupted stitches,

thus, plicating it He then used a single large reinforcing suture to bring the vaginal mucosa on either side of the incision together in the midline, to relieve tension from the plicating sutures He states that he performed the first operation in 1911, and his report was published in the November, 1913, issue of *Surgery, Gynecology and Obstetrics*, the paper having been presented before the American Gynecological Society in May, 1913 Kelly published his description of the operation first in the *Urologic and Cutaneous Review* in June, 1913 In this article he states that he had been performing this operation for the past 10 or 12 years It would thus appear that Kelly not only published his description first, but also performed the operation several years before Baldy

The operation, as performed by Kelly, follows



"H" is the head of the catheter marking the neck of the bladder "GGG" are the guy sutures holding the wound open "S" is the suture at the neck of the bladder re uniting the sphincter muscle

FIG 2—Original Kelly diagram of vesical sphincter plication

'With the patient in the lithotomy position, the posterior wall of the vagina is retracted and the area at the neck of the bladder is brought down with either forceps or guv sutures

"The next step is to slit the vaginal wall down to the urethra and the bladder in the median line for about 1.5 or 2 inches. The neck of the bladder should fall at about the center of the incision. The position of the neck is easily determined at all times by moving the catheter to-and-fro, and feeling its head which presses close up against the urethra. The utmost care should be taken not to cut into the urethra or the bladder at any step of the operation. After making this median incision, the vagina is further dissected off on both sides with tissue forceps and dissected away for a distance of 2 to 2.5 cm around the neck of the bladder. This dissection may be made with blunt pointed scissors which push their way into the tissues, separate the bladder from the vaginal walls and then cut the connecting fibers. The dissection should be deepest at the neck of the bladder.

"When the detachment of vagina from the bladder is completed, the finger should be able to grasp at least one-half or two-thirds of the neck of the bladder, including the contiguous urethra. Sometimes the bladder wall is so thin that its mucosa shines through.

"The next step is to suture together the torn or relaxed tissues at the neck of the bladder, using two or three mattress sutures of fine silk or linen passed from side-to-side. The first suture, taking in about 1.5 cm of tissue, is tied at once when the succeeding suture may be passed outside of this, further contracting and bringing together the tissues at the neck. This is the principal part of the operation, and when done the mushroom catheter ought to be pulled out, the head of the catheter escaping with a little jump as it clears the tightened reconstructed sphincter at the neck of the bladder. The more or less redundant vaginal walls, which have been detached in order to expose the sphincter area, are now resected so that the remaining tissues can be snugly brought together from side-to-side, so as to support the vesical area operated upon and avoid any dead space between bladder and vagina." Kelly's rather crude original illustration is shown in Figure 2.

The operation which we perform today differs somewhat from Kelly's original procedure. It may be noted from Kelly's description that his plication was done only at the "neck of the bladder." He frequently superimposed two or three mattress sutures at that point, but he did not plicate the musculature for the length of the urethra. Our present procedure utilizes the musculature of the full length of the urethra as well as the internal sphincter region.

We are indebted to Kennedy for our knowledge of the sphincter action of the urethra. He studied the urethral mechanism with the aid of radiographs. The bladder was first filled with 200 cc of a 3 per cent solution of sodium iodide. A thin rubber sac was then inserted into the urethra to distend and outline it. The sac was filled with 25 per cent solution of sodium iodide connected with a water manometer at 30 cm of pressure. By taking roentgenograms when the patient was to "hold, relax and void" the action of the urethral sphincter was studied. By studying normal women and patients with various degrees of incontinence, Kennedy concluded that there is an involuntary sphincter about each of the inner and outer thirds of the urethra and an additional sphincter about the middle third of the urethra which is probably under voluntary control. This control, he found to be greater than either of the involuntary muscle controls. He found that if a pressure of 30 cm of fluid stretched the sphincter about the middle third of the urethra, he was justified in suspecting some degree of incontinence. Kennedy also emphasized the importance of adhesions between the urethra and pubic rami. These adhesions he believed to be the result of trauma from the child's head or from previous surgery in the urethral region. Our clinical experience confirms both of Kennedy's conclusions. The presence of sphincters along the entire urethra is confirmed by inspecting the urethra along its entire course through the

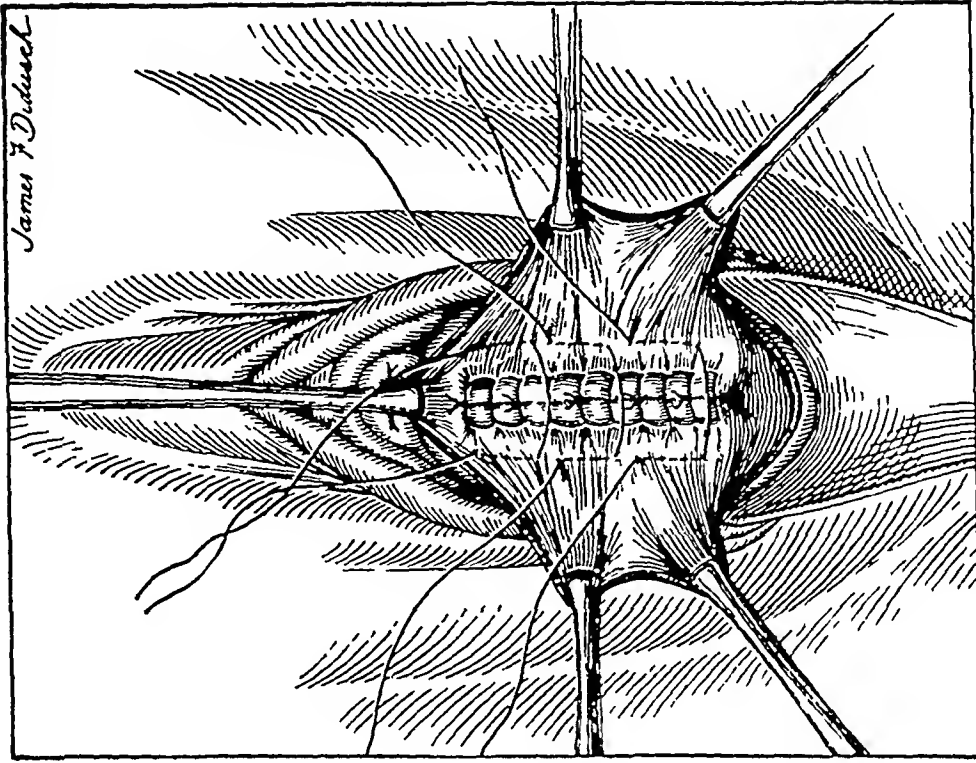


FIG 3-B—Second row of mattress sutures approximating the fascia beneath the urethra

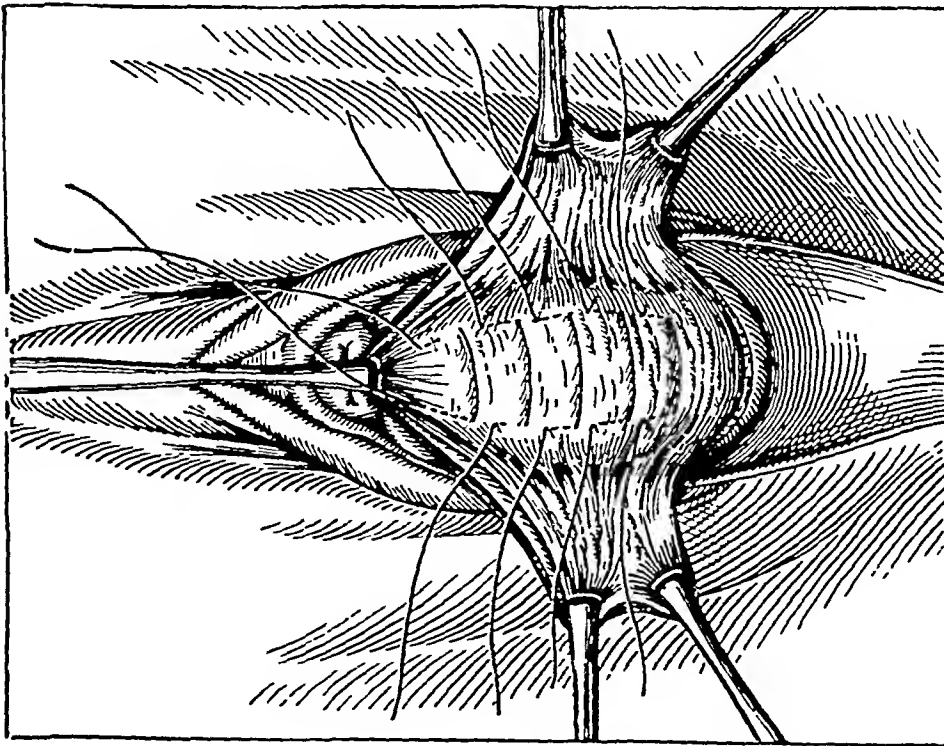


FIG 3-A—Mattress sutures which plicate sphincter fibres from trigone to near the end of the urethra

Kelly and cystoscope. As one withdraws the cystoscope he can notice concentric contractions about the end of the instrument from the trigonal end of the urethra to the meatus. We have also, on occasion, seen evidence of the urethral sphincters being fixed at points by means of periurethral scar tissue. These adhesions have followed childbirth and operative procedures in the urethral regions. Fixed irregular apertures seen on withdrawal of the cystoscope and periurethral scar tissues encountered at operation confirm Kennedy's ideas. However, it is our belief that periurethral adhesions are less frequently a factor in incontinence than Kennedy believes them to be and on the basis of which he devised his operation for the cure of incontinence. We would, then, limit the use of the Kennedy operation to those cases in which periurethral adhesions have been proven by cystoscopic examination.

Kennedy's operation will be briefly described before discussing the one used in this clinic. A midline anterior vaginal incision from cervix to about 1.5 cm from the urethral meatus is made and the vaginal walls separated from the bladder laterally as far as the ramus. "By blunt dissection, the urethra is separated from the median posterior margin of the ramus (keeping extremely close to the ramus) and the separation carried into the paravesical space, which is about 6 cm. The same dissection is repeated on the opposite side, after which the urethra becomes entirely free laterally." The urethral wall is then doubly plicated with mattress sutures for the length of the exposed urethra, which is all of it except the distal 1.5 cm. Finally, three silver wire sutures are placed through the mucosa of the vaginal vestibule close to the margin of the pubic ramus. Kennedy believes that twisting together of these approximates the voluntary sphincter fibers.

The operation done by the author has some of the features of Kelly's original method and some of Kennedy's. If a cystocele is present, an incision is made through the anterior vaginal wall from the cervix to within a half centimeter of the urethral meatus. If there is no cystocele, the incision is carried only the length of the urethra and for about a centimeter beyond beneath the trigone. The vaginal mucosa is dissected laterally, stripping the fascia from it. This fascia is to be used for subsequent plication to form a floor on which the urethra and bladder base rest. If a cystocele is to be repaired, the usual advancement operation is done with plication of the pubovesicocervical fascia in the midline. If there is reason to believe from previous investigation that periurethral adhesions are responsible for the failure of the sphincter to close properly, the urethra is freed extensively laterally, as advised by Kennedy. Otherwise, no attempt at freeing the urethra is made except to expose its inferior surface. A series of mattress sutures of medium silk are taken, beginning about a centimeter beyond the vesical end of the urethra and extending to within a half centimeter of the meatus (Fig. 3, A). When the incontinence is marked, the internal sphincter

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FIG. 4—Miller modification of Goebell-Stoeckel operation. A. Fascial strip has been freed and is split. B. Showing method of encircling urethra.

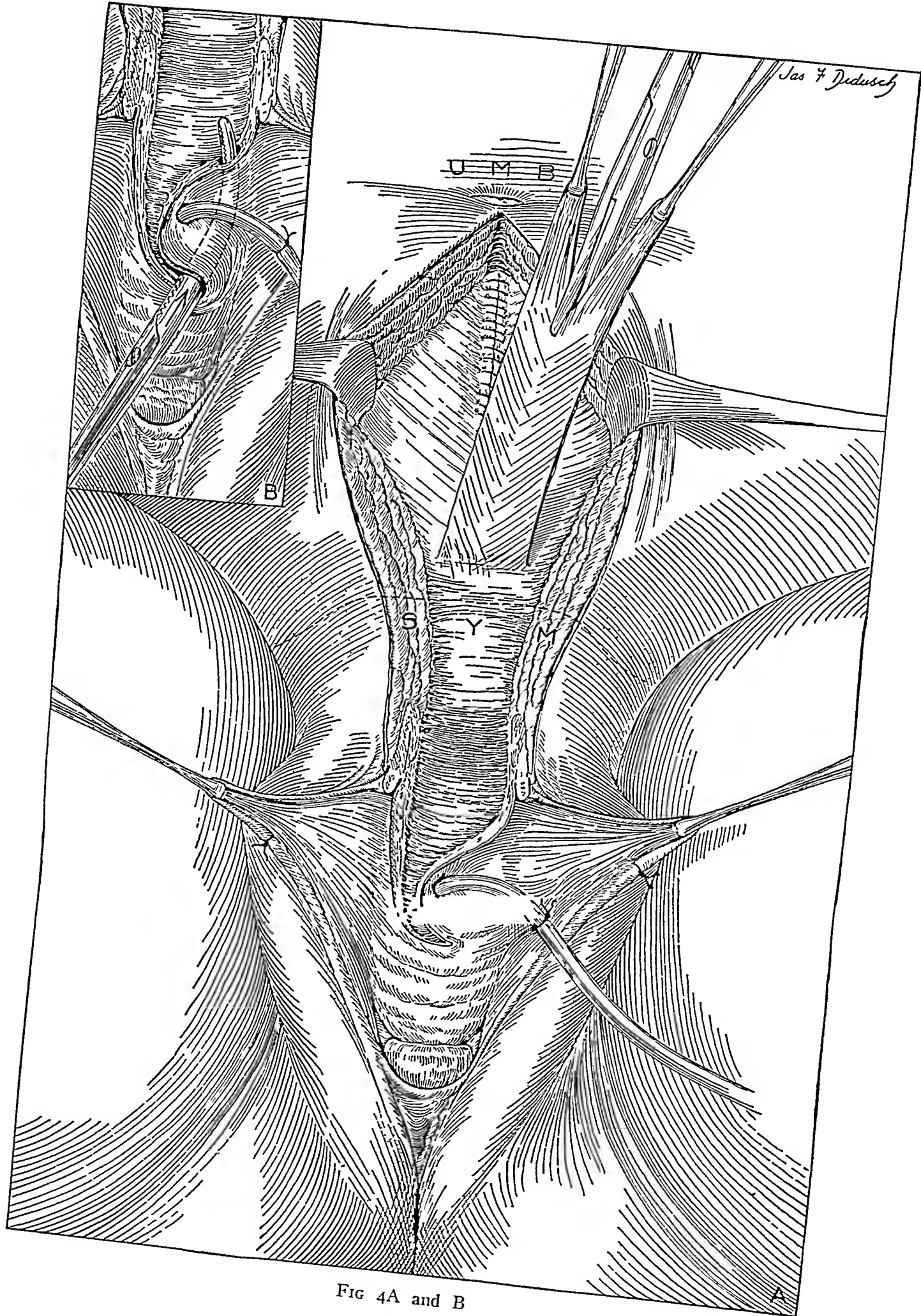


FIG 4A and B

region can be more tightly plicated by taking two or three mattress sutures at that point, as suggested by Kelly, each succeeding suture burying the preceding one. The internal end of the urethra can be identified by the use of a mushroom catheter, but with experience this can be omitted. After the first row of sutures is tied, a second row is placed which invert the first row and approximate the fascia. This restores the floor upon which the urethra rests (Fig 3, B). The excess of vaginal mucosa is excised and the mucous membrane closed with interrupted fine catgut sutures. We prefer not to use an indwelling catheter in order to avoid holding the urethra open. If the patient fails to void, repeated catheterization may be required. If only a simple plication operation is done we do not hesitate to permit the patient to get up to void immediately upon regaining consciousness. If the procedure has been done as part of an extensive vaginal plastic, she is kept in bed 12 to 14 days.

An operation of this type was done on the Gynecological Service of the Johns Hopkins Hospital 249 times during the past ten years. Of these patients, 90.3 per cent reported that they were well, 5 per cent were improved, 3.5 per cent were unimproved, and there was no data on 1.2 per cent. The failures rarely occurred in those cases in which a well-developed urethrocele or cysto-urethrocele was present. They occurred chiefly in those cases in which there was simple sphincter weakness without cystocele, and in cases in which there was a great excess of scar tissue about the urethra as the result of previous operations. The subsequent treatment of the failures will be considered later in this paper.

#### THE GOEBELL-FRANGENHEIM-STOECKEL TYPE OF OPERATION

From the above report it is obvious that we must search further for a cure of some cases of stress incontinence. After one or more unsuccessful plications, scar tissue may make further plication futile. Also, in those cases in which the urethra and sphincter mechanism have been destroyed, the reconstructed urethra has no contractile power, and this must be supplied from some other source. Finally, in certain neurologic bladders with incontinence, there is the possibility that a new sphincter mechanism can be supplied which will function sufficiently well to give the patient control.

For many years past, surgeons and urologists have attempted to supply sphincter action by transplanting muscle from without. Martius<sup>8</sup> used the bulbocavernosus, Deming<sup>9</sup> the gracilis, and others utilized part of the levator ani muscles. Although some successes have been reported, there were many failures and most of these operative attempts are only of historic interest. The operations of this type which are done today are chiefly modifications of the Goebell-Stoeckel technic, first described in 1910. In that year, Goebell<sup>10</sup> reported on the transplantation of the pyramidalis muscles retropubically, encircling the posterior urethra. In 1914, Frangenheim<sup>11</sup> modified Goebell's technic by utilizing a strip of rectus fascia from the midline, to which the pyramidalis muscles were attached. Stoeckel<sup>12</sup> was the first to combine the Goebell-Frangenheim strap technic with a vaginal plastic procedure. Norman



Miller<sup>13</sup> objected to bringing the strap of fascia down retropubically because of the possibility of hemorrhage and bladder injury in the inaccessible retro-pubic space and accordingly modified the Goebell-Stoeckel operation by bring-



FIG 4—Miller modification of Goebell-Stoeckel operation

C Fascial strips have been brought down and will be sutured beneath the urethra

ing the fascia down anterior to the symphysis (Fig 4, A, B, C) The first operation of this type performed in our clinic was done according to Miller's modification and an excellent result was obtained, but we have abandoned this modification because one is able to get a more direct pull on the posterior



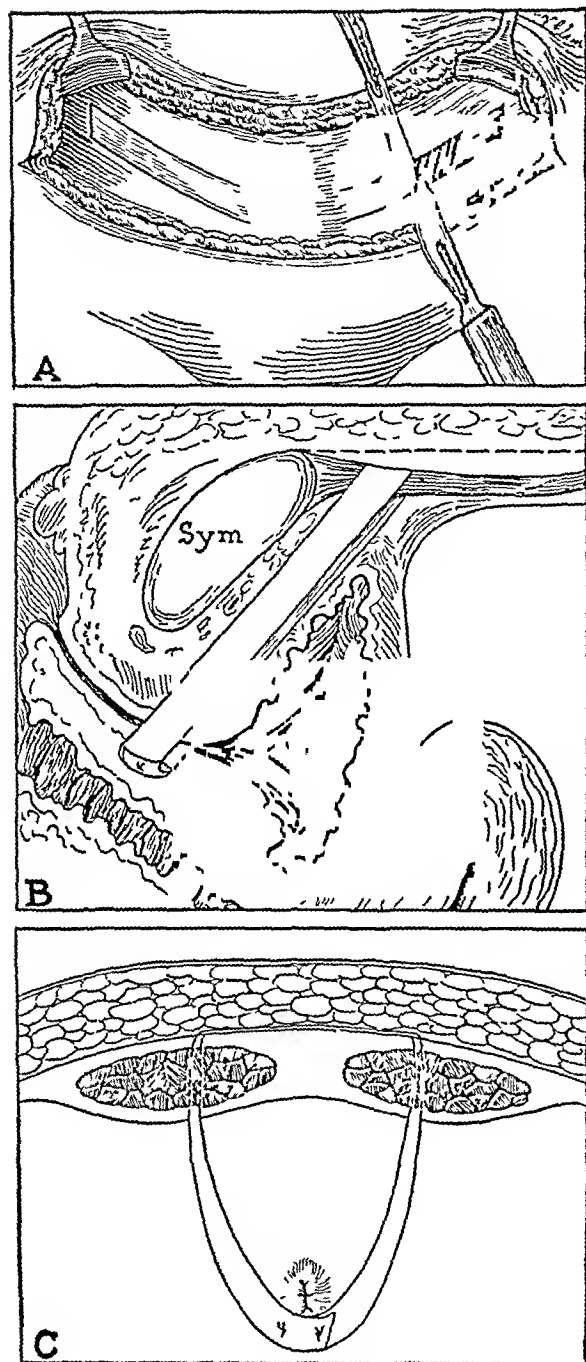


FIG 5—Aldridge modification of Goebell-Stoeckel operation for urinary incontinence

A Fascial strips are being separated through a Pfannenstiel incision

B Fascial strips shown in position around posterior portion of urethra. Dotted line indicates position of rectus muscles when contracted

C Diagram indicating slinglike action of the fascial strips

urethra by the retropubic route. Nor have we injured the bladder or encountered hemorrhage by tunnelling retropubically. In 1942, Aldridge<sup>11</sup> modified the procedure by making a transverse semicircular abdominal incision and cutting bilateral straps of fascia obliquely upward and outward. The straps which are left attached at the medial ends then are made to pierce the rectus muscles as they are brought down behind the symphysis (Fig 5). There is one obvious advantage to the bilateral straps in those cases in which there is an old midline scar. Aldridge also believes that the spring obtained from the rectus muscles in their normal positions is far better than one could obtain from the displaced pyramidalis muscles.

We have performed operations of this general type 13 times in our clinic during the past ten years. Since 1942, we have generally used Aldridge's modification, which appears to have the advantages claimed for it by its author. Our series is small, which indicates that we have selected our cases with care. It is easy to become over-enthusiastic about this procedure but we have restrained ourselves when we believed a lesser operation would suffice. For example, if a woman who has had previous unsuccessful surgery for stress incontinence presents herself with a well-developed cysto-urethrocele, we do

not proceed with this operation. It is obvious that she has not had proper vaginal plastic work done, and we repeat it with urethral plication. If the Goebell-Stoeckel operation were done routinely for such cases, the percentage of cures would be in the neighborhood of 100 per cent. In all of the cases in our series in which the operation was done for stress incontinence following failures at plication, the operation was successful, with a single exception. This failure was apparently due to a great excess of scar tissue resulting from previous attempts at plication. On the other hand, more recently, a perfect result was obtained in a similar case, using the Aldridge modification. Sphincter function was given to two patients with spina bifida occulta and to one with a mild tabetic bladder. Neurologic bladders should be selected for this operation with the greatest of care. They should be subjected to cystometric examination before a decision to operate is made. Operations of the Goebell-Stoeckel type should be restricted to those cases in which there is a relaxation of the involuntary sphincter and an absence of voluntary sphincter control. The bladder should not be too spastic as the expulsive power of the spastic bladder would probably overcome the added resistance offered by the transplanted fascia.

The Goebell-Stoeckel type of operation failed to cure all three of our patients upon whom a plastic operation had been done previously to form a urethra. In one case the entire urethra had sloughed following a difficult delivery. In the second there was a congenital absence of urethra and seven previous attempts had been made to create a urethra and restore continence. In the third case the whole urethra and part of the bladder wall had been eaten away by lymphopathia venereum. Failure in these three instances can be attributed to several factors. The absence of *any* normal sphincter mechanism places more responsibility upon the strap for complete sphincter action. Apparently, the strap often fails in this. The urethra which is formed by the plastic procedures is usually too short to serve as an adequate tube against which the strap can make pressure. The artificial urethra is also usually too thin for surgical dissection without perforating into the lumen, and it contains so much scar tissue that postoperative sloughing may occur after attempting the strap operation. In the case of the healed lymphopathia the tissues were still the site of chronic edema and fibrosis, making surgical manipulation very difficult and healing uncertain because of lack of blood supply.

The modified Goebell-Stoeckel operation as done in our clinic follows:

The position of the patient on the table is important. She is placed in a modified lithotomy position with the thighs not too acutely flexed on the abdomen. In this position the abdominal wall may be exposed and the patient will not require redraping for the vaginal work. A complete clean-up of the abdomen and vagina is done before draping. The perineum is temporarily covered by a sterile towel which is removed at the beginning of the vaginal part of the operation. Likewise, the abdominal wound is closed after the fascial straps are cut, except for a small segment in the midline, and the

wound covered with a sterile towel held in position by towel clips to prevent contamination while the vaginal operation is being done

A semicircular transverse lower abdominal incision is made through the panniculus, the aponeurosis is cleared of fat over an area about one inch wide and bleeding is controlled

The strips of fascia are cut on either side of sufficient length to be carried down retropubically and encircle the urethra. The length of these strips, naturally, must be estimated and will vary, depending upon the width of the symphysis pubis, but if they are carried up to the level of the anterior superior spines of the ilia they will be of sufficient length, even though the symphysis is quite wide. The strips will be composed of the aponeuroses of both external and internal oblique. They are separated from the subjacent muscle and, thus, mobilized down to their bases. The medial end of each strip is left attached at about 1.5 cm from the midline. The incisions in the aponeuroses are then closed with continuous sutures of No. 1 chromic catgut, the fat approximated with interrupted sutures of double zero chromic catgut and the skin closed with continuous fine silk, leaving a small unclosed space at the lower portion of the incision. The fascia strips are placed in this space and covered with moist sponges. The closed portion of the abdominal wound is covered with sterile towels.

The operator is then seated for the vaginal portion of the operation. The labia minora are sutured laterally for good exposure and a posterior retractor placed in the vagina. An Allis clip is placed in the urethral meatus and a second one in the midline on the vaginal wall about six centimeters back from the first. A midline incision is then made through the vaginal mucosa, extending from about 1 cm from the urethral meatus back for about 5 cm. The vaginal mucosa is dissected laterally and the fascia stripped from it. If the operator intends to combine the Goebell-Frangenheim-Stoeckel procedure with urethral plication, this is done as previously described.

No attempt is made to dissect digitally lateral to the urethra, as suggested by Aldridge and Studdiford<sup>15</sup>. The author does not believe that this is necessary and bleeding may be avoided by omitting it. However, the index finger of the left hand is placed at the left side of the urethra. Then, using a long Kelly clamp in the right hand, the space of Retzius is entered from above by penetrating the rectus muscle at the base of the fascial strip. The point of the clamp is directed downward and against the periosteum of the symphysis. By taking this precaution the author has never perforated the bladder or had any persistent hemorrhage. In most cases, the bleeding is *nil*. The Kelly clamp is then forced down lateral to the urethra, aiming at the tip of the left finger below. In some instances, the fascia at this point is so tough that it is perforated with difficulty by the blunt Kelly clamp but a small cut with the scalpel directly over the point of the clamp permits it to perforate. Then the clamp is opened slightly and a second clamp, similarly opened, is fed into the jaws from below. Both clamps are shut and traction made on the upper clamp as the lower clamp is pushed. Then the end of the left fascia strip is fed into the

jaws of the lower clamp and the clamp withdrawn from below. This is repeated on the opposite side, and, thus, the ends of both strips are delivered beneath the urethra. The straps are over-lapped slightly, any excess is cut off, and the strips sutured together with three or four interrupted sutures of medium silk. Care is taken to get the proper amount of tension on the straps to give the patient continence. This is tested by distending the bladder through a glass catheter and making moderate suprapubic pressure. The excess of mucosa is excised and the vaginal wound closed with interrupted sutures of No. 0 catgut. The small midportion of the abdominal wound is then closed. We prefer not to use an indwelling catheter, but if the patient fails to void spontaneously within several days, we occasionally resort to it.

#### VESICOVAGINAL FISTULA

The subject of vesicovaginal fistula dates from antiquity. Since the literature contains many historical sketches of the subject, no attempt at such a review will be made here, but reference will be made to a few of the milestones in the development of our present operative knowledge. No one man is responsible for this knowledge, it having been acquired step-by-step through the tireless efforts of surgeons dating back to the 17th century. Before that time the condition was considered hopeless and one sees references even as late as the middle of the 18th century to the treatment of these fistulae by the wearing of a pulverized toad in a little bag over the pit of the stomach. The more practical-minded of these times devoted their efforts to making receptacles to catch the urine, and, thus, make the life of the victim more endurable.

The first real surgical contribution was made by a Hollander, H. Van Roonhuyse,<sup>16</sup> whose contributions were far in advance of his time and apparently overlooked by many later writers who fumbled about with much less rational methods. In 1672 Van Roonhuyse recommended

The placing of the patient in a position appropriate for lithotomy

The satisfactory exposure of the fistula by a retracting speculum

The thorough denudation of the margins of the fistula

The approximation of the denuded edges by means of quills thrust through the edges of the wound and held in place by silk threads

The dressing of the wound with balsam and absorbent vaginal dressings

The patient kept quiet in bed until the parts had healed

There is no report of Van Roonhuyse's successes and failures but Johannas Fatio<sup>17</sup> of Basel reported on two cases successfully operated upon by him in 1675 and 1684. He states that he employed the "method of the skilled physician, Van Roonhuyse."

Little progress was made after that until 1839, when George Hayward,<sup>18</sup> at the Massachusetts General Hospital, reported nine cases in which he described the important technical point of detaching the vagina from the bladder. Then came ether anesthesia, and it was probably used for the first time for this operation by Hayward, in 1847. In 1846, Metzger,<sup>19</sup> of Prague, described using an instrument very much like the Sim's speculum. In 1847,

John Mettauer,<sup>20</sup> of Virginia, first used twisted metal (lead) sutures. In 1852, Wutzer,<sup>21</sup> of Bonn, reported curing 11 out of 35 patients. He first used suprapubic drainage.

In 1845, Jobert de Lamballe<sup>22</sup> described his incision for relieving tension on the fistula suture line. It consisted of a transverse vaginal incision anterior to the cervix, whereby the bladder could be freed from the cervix. Gustav Simon,<sup>23</sup> who was a pupil of Jobert, and appreciated the value of easing the tension on the suture line, attempted to do this by the use of tension sutures instead of incisions.

Marion Sims<sup>24</sup> first paper on vesicovaginal fistula appeared in 1852, and it is generally conceded that he is the father of surgery for vesicovaginal fistula in America. There is no doubt that he attained greater success than anyone up to his time. It is interesting to note, however, that his operation was not new. Each step had been used and described before by the surgeons mentioned above, and others. The only innovation which Sims contributed was the use of silver wire. This was, in truth, one of the greatest contributions and Sims guarded his priority with such jealousy that he devoted most of his anniversary oration before the New York Academy of Medicine, in 1857, to defending it. He declared it to be "the most important contribution as yet made to the surgery of the present century."

"The only thing comparable to it is etherization, and in practical results of permanent benefit, it is absolutely contemptible, when compared with those from the universal use of silver sutures in the broad domain of general surgery."

Since the time of Sims there have been changes and refinements in technic but nothing revolutionary. These points will be discussed in considering the principles which we have used in operating upon these reported cases. The present series consists of 41 patients with vesicovaginal fistula upon whom we have operated during the past ten years.

*Causes and Prevention*—Much can be learned about the prevention of vesicovaginal fistulae by a study of the causes. We have listed the causes in Table I.

TABLE 1  
41 CASES OF VESICOVAGINAL FISTULA

Causes	Number of Cases
Vaginal delivery	8
Rupture of uterus, bladder and vagina following pituitrin during labor	1
Total abdominal hysterectomy	15
Subtotal abdominal hysterectomy	2
Radium treatment for carcinoma of cervix	3
Radium treatment for benign bleeding	1
Radium and total hysterectomy for carcinoma of cervix	3
Manchester operation	1
Colpotomy	1
Cesarean section	1
Vaginal removal of cervical stump	3
Automobile accident	1
Biopsy bladder tumor	1
Total	41

The striking thing noted is the low incidence of fistulae due to vaginal deliveries and the high incidence due to total abdominal hysterectomy. Fifty years ago obstetrical injuries were responsible for more fistulae than all other causes combined. Due to the improvement in obstetrics the incidence of fistulae due to deliveries has been reduced to a minimum (Eight out of our 41 cases). On the other hand, within the past decade there has been a tremendous increase in fistulae resulting from total abdominal hysterectomies (15 of our 41 cases). This is the result of a great swing toward total hysterectomy on the part of American operators. Many publications from the larger gynecologic clinics have advocated routine removal of the cervix whenever the uterus is removed. As a result of this many surgeons have adopted this practice who lack the experience or surgical skill to do the operation expertly. From this source come most of the vesical fistulae seen today. It is not the purpose of this paper to discuss the relative merits of total and subtotal hysterectomy, but it behooves every inexperienced surgeon to take council with his conscience before performing the total operation in cases where the lesser procedure will cure the patient. It is true that vesicovaginal fistula does occasionally occur as a sequel of a very difficult subtotal hysterectomy, as is shown in this series, but bladder damage in the run-of-the-mine subtotal hysterectomy is inexcusable.

The five cases in the series in which vesicovaginal fistula followed irradiation for cervical cancer does not represent the total number of fistulae occurring in our Radium Clinic but only those cases in which repair was attempted. In two cases irradiation and total hysterectomy preceded the fistula. In one of these the cause was obviously irradiation, for the fistula appeared 11 years after the surgery and irradiation. In the other it was impossible to be certain which of the two factors was responsible for the fistula.

The three cases of fistula following vaginal removal of the cervical stump are worthy of note. One of these cervixes was removed by electrosurgical means and the others by scalpel. It is our belief that, generally, it is a safer procedure to remove a cervical stump transabdominally, if a complete removal is desired. If a partial removal is all that is required, it can safely be removed *per vaginam* with the electrosurgical instrument. As a result of peritonealizing the cervical stump at the time of the subtotal hysterectomy, the bladder is often intimately bound to it, so the more or less blind dissection from below is hazardous to the bladder.

**RESULTS** Of the 41 patients with vesicovaginal fistula, excluding those with complete destruction of the urethra, 37 were cured. The results are shown in Table II.

In two of the successful cases, three operative attempts were made in our clinic before the fistula was finally closed, in seven cases two attempts were necessary and in the rest the closures were successful as a result of our first attempt. Only 15 of the 41 patients came to us for the first attempt at closure. Eleven had had one previous attempt, eight had had two previous attempts,

four had had three attempts, and three had been operated upon unsuccessfully seven times before coming to our clinic

TABLE II  
RESULTS OF SURGERY ON 41 CASES OF VESICOVAGINAL FISTULA

	Name	Previous Attempts	Operations on Our Service	Result
1	M T	None	1 vaginal	Well
2	J F	2 1 shortly after delivery, 1 a year before admission	1 vaginal	Well
3	B V	1 3 months after occurrence	3 1st—abdominal 2nd—vaginal 3rd—vaginal	Well
4	A F	2 1 two weeks after occurrence and another 6 years later	1 vaginal	Well
5	E R	None	2 complete closure of vagina	Well
6	F L	1 5 months after occurrence	1 vaginal	Well
7	L J	1 6 weeks after occurrence	3 vaginal	Well
8	H E	2	2 1st—abdominal 2nd—vaginal	Well
9	M F	1 5 months after occurrence	1 vaginal	Well
10	H M	None	1 vaginal	Failure
11	E R	None	1 vaginal	Well
12	O D	3 at monthly intervals beginning 1 month after occurrence	2 vaginal	Well
13	F R	None	1 vaginal	Well
14	D G	1 7 months after occurrence	2 vaginal	Failure
15	M H	1 4 months after occurrence	1 vaginal	Well
16	G H	None	1 vaginal	Well
17	D H	2 6 years before admission vaginal and abdominal	1 abdominal	Well
18	E T	7 4 abdominal and 3 vaginal over 4 years	1 vaginal	Well
19	J Mc	None	1 vaginal	Well
20	G S	1 2 months after occurrence	1 vaginal	Well
21	D H	1 2 months after occurrence	1 vaginal	Well
22	B H	None	1 vaginal	Well
23	D T	3 1 month, 3 months, 16 months after occurrence	1 vaginal	Well
24	E S	None	2 vaginal	Well
25	E B	2 1 vaginal 5 months after occurrence and intra abdominal 1 month later	1 vaginal	Well
26	R C	7 Between 1938 and 1943	1 vaginal	Well
27	E D	1 Abdominal	1 vaginal	Well
28	R P	None	1 vaginal	Failure
29	Y B	1 2 years after occurrence	1 vaginal	Well
30	K N	7 1st 2 months after occurrence, next 3 attempts in 3 months	1 vaginal	Well
31	E R	2	1 vaginal	Well
32	M H	3	2 1st—abdominal 2nd—vaginal	Well
33	N J	None	2 vaginal	Failure
34	E C	None	1 vaginal	Well
35	P L	None	1 vaginal	Well
36	A W	1 vaginal 5 months after occurrence	1 vaginal	Well
37	R N	2 1st 1 year after occurrence, 2nd 2 weeks later	1 vaginal	Well
38	N J	3 1 abdominal 9 days after delivery, 2 vaginal	1 vaginal	Well
39	K D	None	1 vaginal	Well
40	R G	2 1st 5 months after occurrence, 2nd shortly after	1 vaginal	Well
41	E K.	None	1 vaginal	Well

#### PRINCIPLES OF VESICOVAGINAL FISTULA SURGERY

There is no field in surgery in which the operator is thrown more completely on his own resources than when he is dealing with a vesicovaginal fistula. Each case is a problem unto itself, and often the operator must impro-

vise rather than carry out his previously carefully planned operation. Hence, in this paper no attempt will be made to describe typical operations but principles will be discussed which we feel have contributed to the success of this series of difficult operations. Even though some of these principles are old they will bear repetition, for it is obvious from the number of failures to cure vesicovaginal fistulae that they are often not applied.

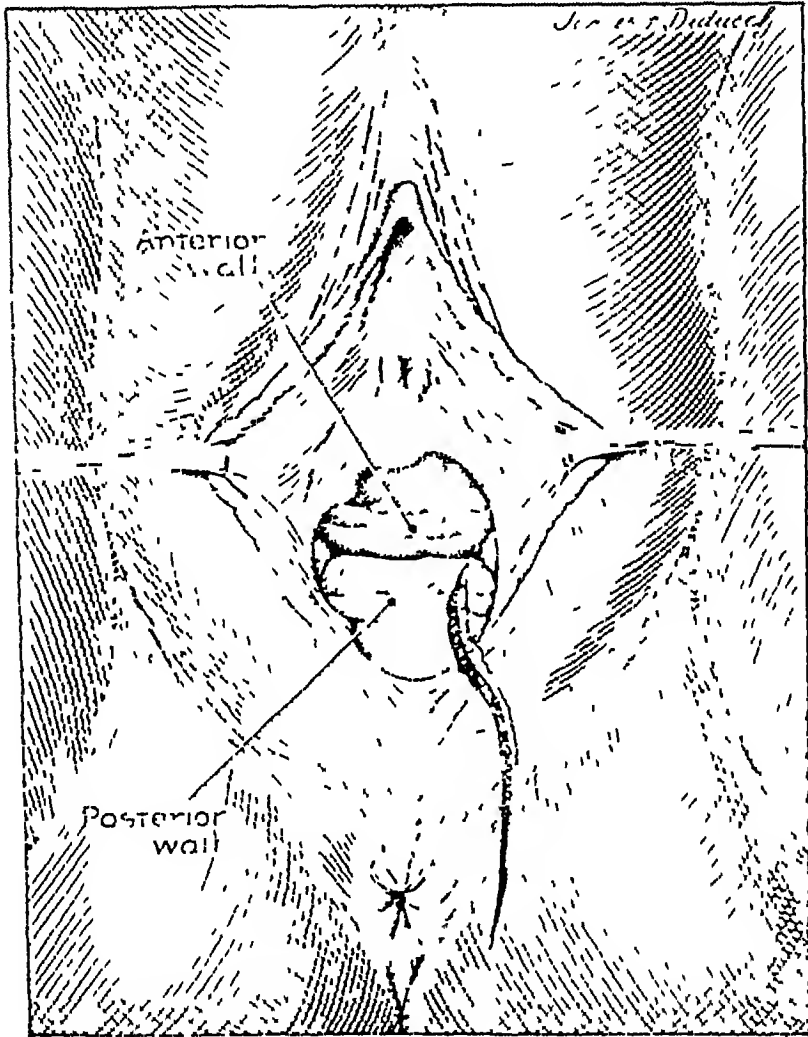


FIG 6—Schuchardt incision

The advantage of having the tissues in the best possible condition before attempting closure is great. After the occurrence of a fistula, five or six months should elapse before surgery is attempted. Hunner has emphasized this repeatedly but a glance at Table II will show that many operators do not observe this rule. After this first failure, the surgeon often makes another attempt, sometimes within a few weeks. Possibly a sense of guilt in having had a hand in forming the fistula urges him to try again and again before the edema and infection of the previous operation have subsided. Each failure increases the amount of scar tissue and decreases the patient's chances of an ultimate cure. The situation should be explained to her, and in most instances



she will gladly wait to better her chances of ultimate cure. While the patient is awaiting surgery, she should be instructed to take sitz baths and to irrigate the vagina with potassium permanganate solution (1-8,000) or with a weak vinegar solution. This prevents and dissolves urinary salt incrustations and, in general, improves the condition of the tissues.

The approach to the operative field should be given considerable thought. More and more we favor the vaginal approach. In this series the abdominal approach was used only five times, and it should be noted that only one of these was successful. In the other four cases the fistulae were cured by a second vaginal operation. Almost never is an obstetrical fistula approached to advantage by the abdominal route. Formerly, we occasionally attacked a high postoperative fistula through the abdomen but by using the Latzko vaginal method we believe it will rarely be necessary in the future. About the only time it will be necessary to resort to the abdominal route will be in those cases in which the high fistula is inaccessible vaginally because of previous operations making the vagina narrow and rigid. Before giving up the vaginal approach, one should always remember that a deep vagina can be made relatively shallow by the Schuchardt incision (Fig 6). Most of our vaginal operations are done with the patient in the lithotomy position but occasionally we use the Sims' left lateral or the knee-chest position.

Special attention should be directed to the Latzko method of closure of high vesicovaginal fistulae. It is particularly important for surgeons to recognize and use this procedure because it is so well adapted to the everincreasing number of fistulae following total hysterectomy. In 1933,<sup>25</sup> Latzko described partial colpocleisis for fistulae following panhysterectomy. The method is illustrated in Figure 7. The procedure is usually relatively simple to execute and we have had no failures in closing these postoperative fistulae since we have used it. Inasmuch as these fistulae are at the apex of the vagina, the amount of vaginal shortening is negligible, unless the fistula has been greatly increased in size by previous unsuccessful operations. In one of the above cases in which there had been seven previous attempts at closure, it was necessary to close the upper two-thirds of the vagina. Although this is undesirable, the inconvenience is nothing compared to that of the preexisting incontinence. I am convinced that this particular fistula could not have been closed by any other method.

Although the *sine qua non* for the use of the Latzko technic has always been that the patient's uterus be previously removed, we have recently found

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FIG 7—Typical Latzko operation for closure of post-panhysterectomy vesicovaginal fistula

- A Line of incision
- B Denudation of vaginal mucosa
- C Anterior and posterior vaginal mucosa has been removed
- D First layer of interrupted mattress sutures
- E Second layer of sutures
- F Closure of vaginal mucosa with silver wire sutures
- G Completed operation

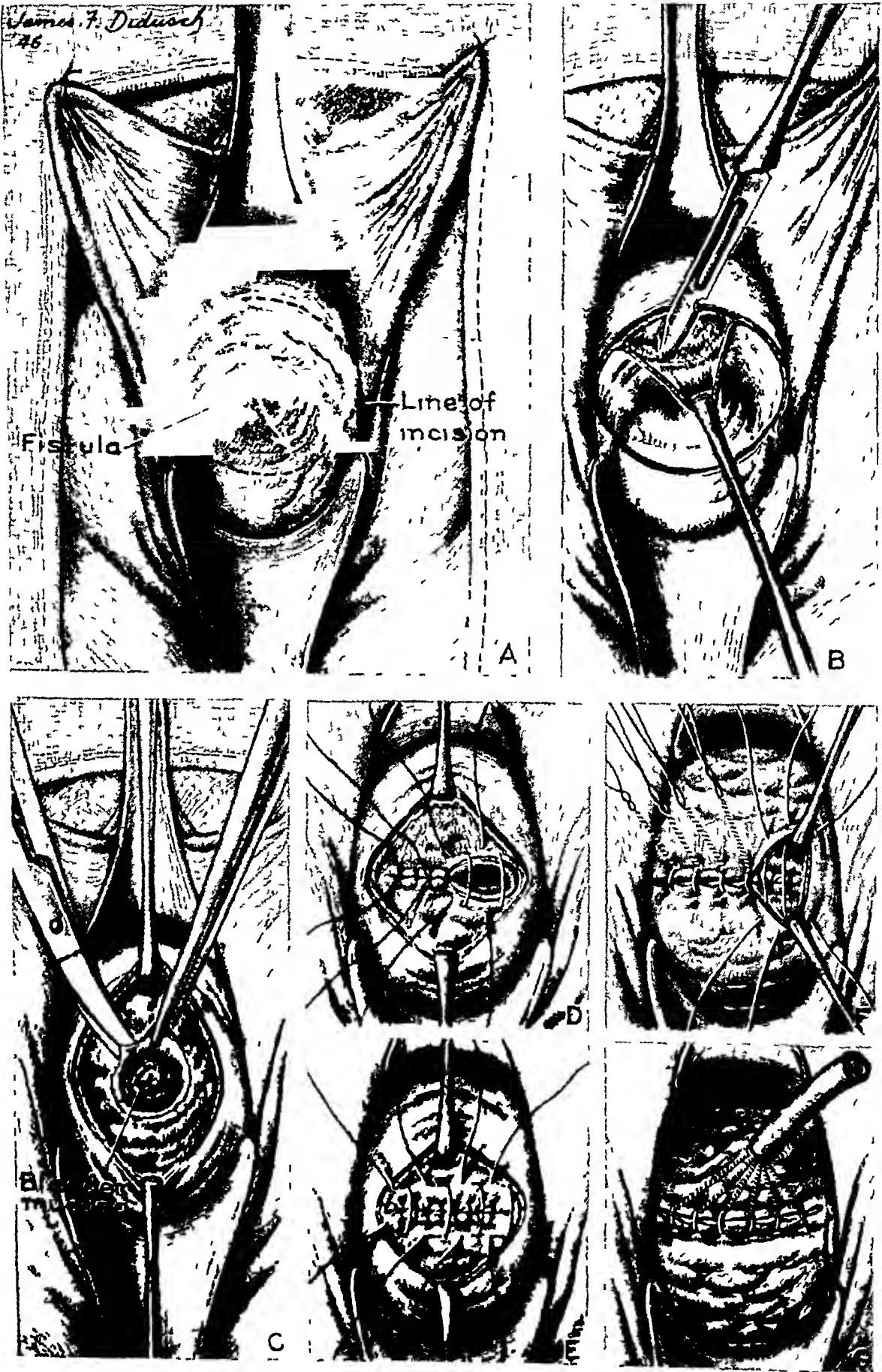


FIG 7  
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an extension of its use, which is illustrated in three cases in this series. In these three cases the patients had been treated by irradiation for cervical cancer several years before. The cancer had been completely cured and the cervix totally eradicated by the radium, but the patients were left with large vesicovaginal fistulae. The extreme scarring so fixed the tissues that the condition would have been quite inoperable by any other technic. Denuding the vaginal mucosa both anteriorly and posteriorly and approximating the

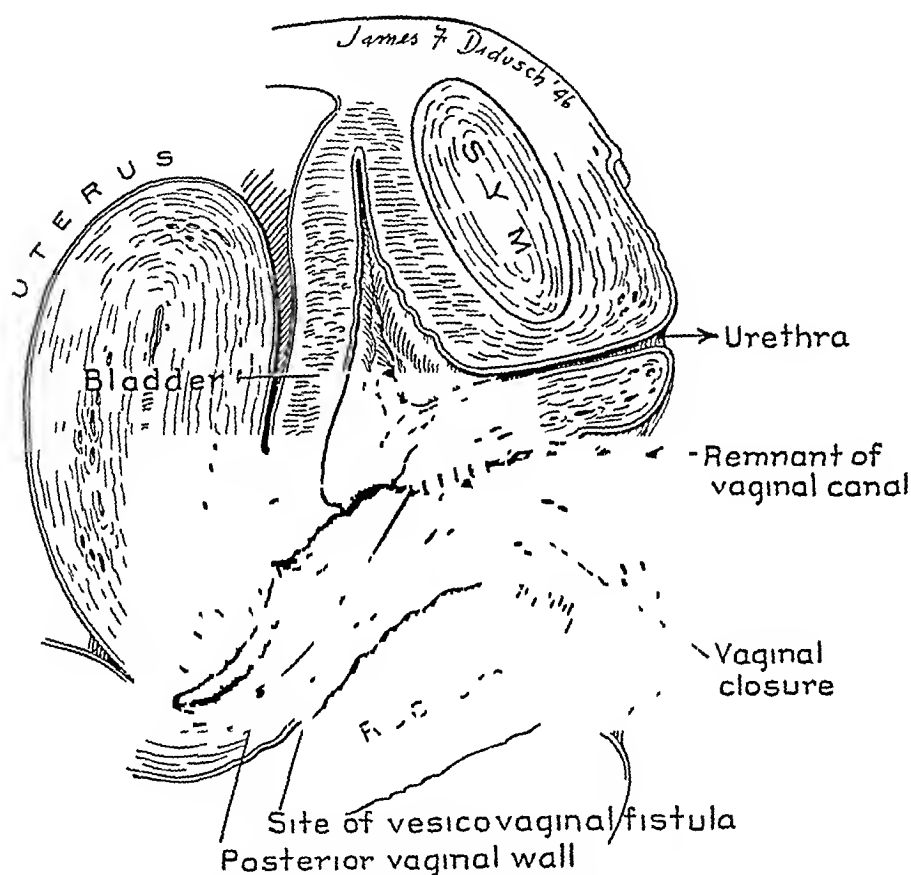


FIG 8—Demonstrating use of Latzko principle of partial colpocleisis for cure of vesicovaginal fistula in the presence of a cured cervical cancer

vaginal walls over a broad area cured two of the three cases (Fig 8). Including the obliterated cervix in the bladder apparently is quite innocuous. The third patient still has slight leakage. Although this procedure is applicable in only a small percentage of irradiation fistulae, it can give relief to a selected few women.

Before leaving the subject of the approach to the operative field, I should like to say that I have never seen a vesicovaginal fistula which seemed to be best approached transvesically, as practiced by some urologists. It is difficult for us to conceive of a case in which this would be advantageous.

## URINARY INCONTINENCE IN WOMEN

In general, we prefer to close fistulae vaginally with the split-flap technic and approximate broad surface to broad surface. After dissecting the vaginal mucosa free, for about two centimeters around the circumference of the fistula, the edge of the bladder opening is inverted into the bladder, using a running Cushing stitch or an interrupted stitch of the same type (Fig 9 B). In the more difficult cases the interrupted stitch is usually advantageous. Fine catgut should be used for this and, in tying, the tissues should be approximated but not strangulated. After the first suture line is placed, the bladder

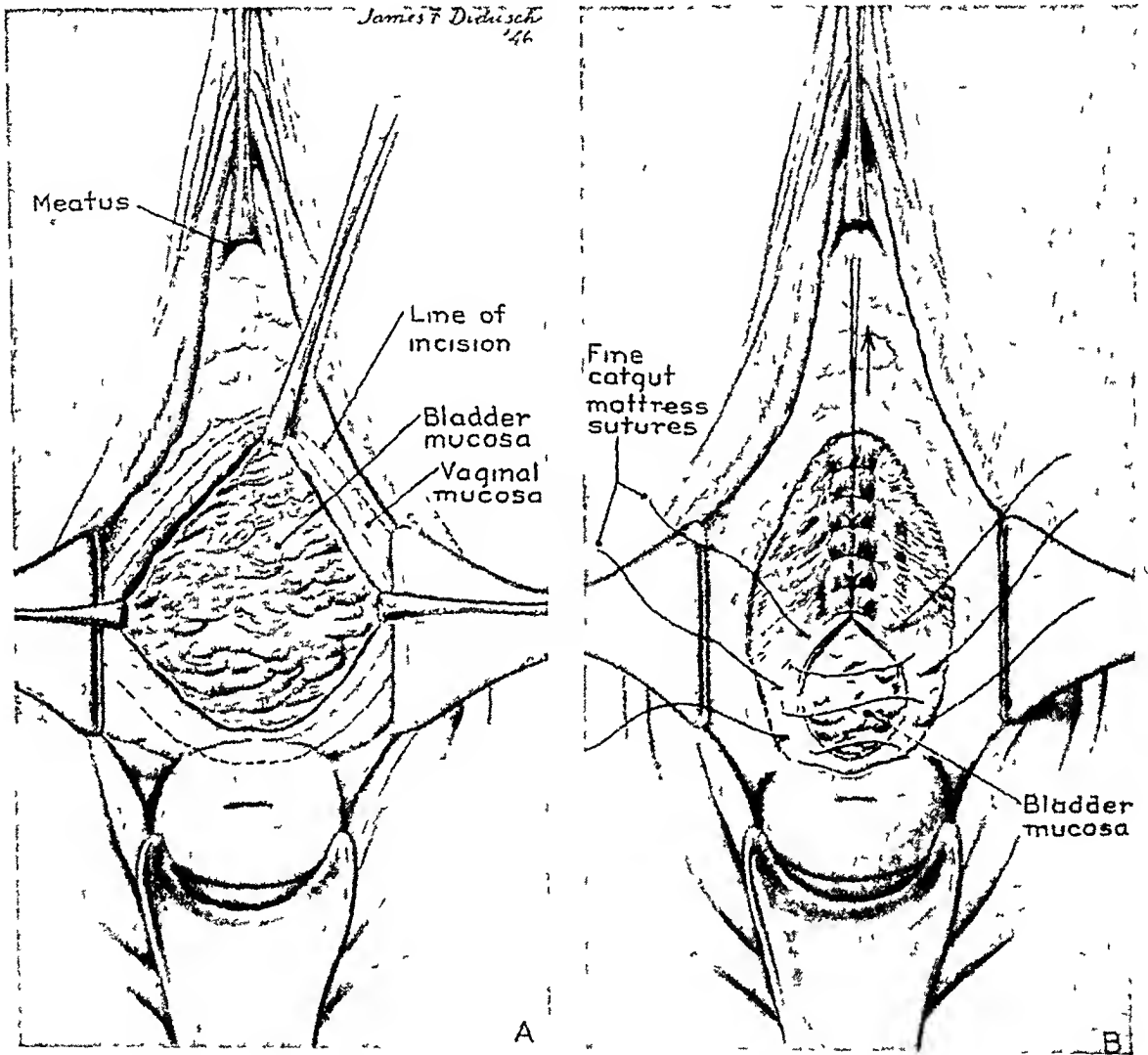


FIG 9—Closure of large vesicovaginal fistula

A Showing defect and line of incision

B Showing method of placing first layer of interrupted catgut sutures, inverting edge into bladder

closure is tested. For this we use a weak solution of sterilized milk. This was first demonstrated to me by Guy Hunner. It is far superior to methylene blue solution because, if there is very slight leakage, a drop of the milk stands out very plainly against the bloody background. In addition, the milk does not stain the tissue, as does methylene blue solution. This is a distinct advantage if there is much leakage and if one is working at some depth where illumina-

tion is difficult. If leakage is demonstrated, further closure is done. If there is no excessive tension, a second line of sutures may be used to approximate the raw surfaces. However, if a second suture line has a tendency to result in too much tension, it is best omitted. The ragged avascular and scarred vaginal mucosa is then trimmed in order to be sure of good blood supply for healing. In the simple cases fine catgut may be safely used for suturing the

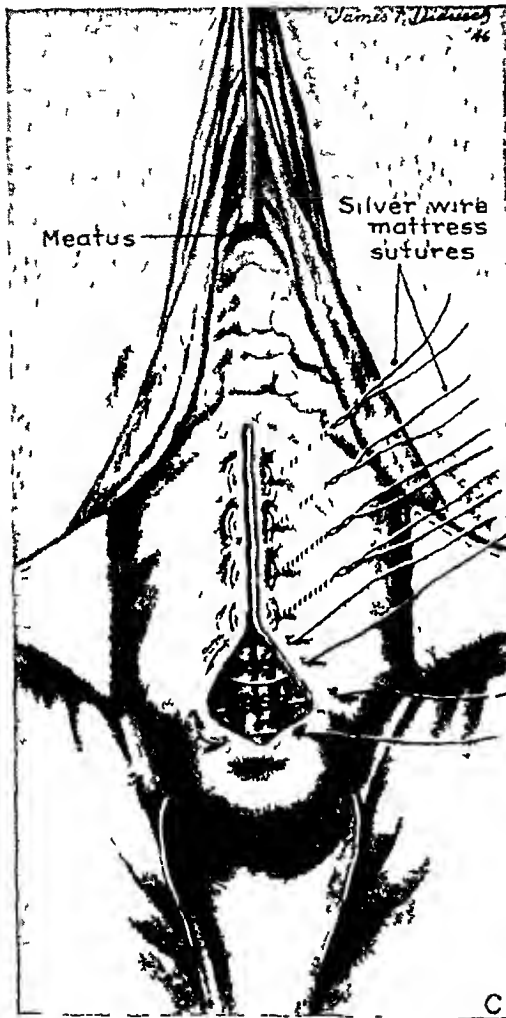


FIG 9—Closure of large vesicovaginal fistula

C Closure of vaginal mucosa with interrupted mattress sutures of silver wires everting mucosa. Note that sutures pick up subadjacent tissues to close dead space.

drainage. Occasionally, we close a simple fistula and permit the patient to get up to void immediately after recovering from the anesthetic. If she is unable to void, we prefer an indwelling catheter to repeated catheterization. In the difficult cases we believe bed rest up to two weeks is advisable and during this time foolproof drainage is essential. To provide this we frequently provide double drainage in the form of a therapeutic vesicovaginal fistula or suprapubic

vaginal mucosa, but in the difficult cases where there is excessive scar tissue from previous operations and, perhaps, a little more tension than desirable, there is no suture material equal to No. 26 silver wire. It can be left in place for two weeks or longer as its resistance to infection in this unclean field is truly remarkable. Although I cannot go quite as far as its discoverer (J. Marion Sims) and claim it as a greater discovery than etherization, I have great enthusiasm for its use in difficult fistulae. I prefer to place it as a mattress suture, everting the mucosal edge and approximating broad undersurface of the mucosa to broad surface. When these sutures are placed, I also like to pick up a bit of the subadjacent tissue to obliterate dead space (Fig. 9C). When conditions are such that a double-layer closure is impossible, silver wire is admirably suited for approximating the tissues in a through-and-through manner. In such cases tension can often be released by making a properly placed relaxing incision through the mucous membrane.

Many a perfectly executed operative closure is ruined by improper postoperative care. The essential point in postoperative care is bladder

## URINARY INCONTINENCE IN WOMEN

drainage in addition to the indwelling urethral catheter. Then, if one route becomes stopped, the other will provide drainage. If there is ample space above the level of the trigone, we prefer vaginal cystotomy. A mushroom catheter is inserted through a short midline vaginal incision and sutured in place with a heavy silk suture (Fig 10). In the more difficult cases in which previous attempts have been made the anterior vaginal wall may be so scarred

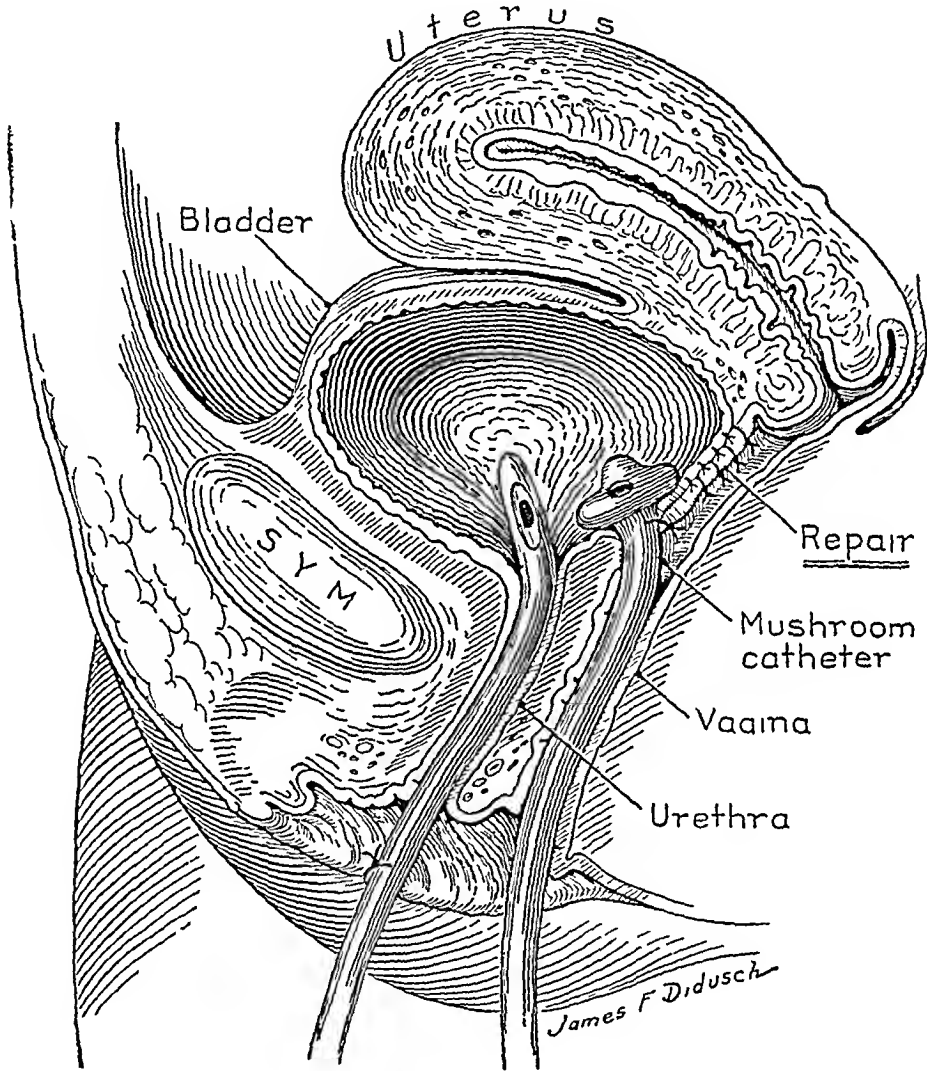


FIG 10—Double bladder drainage through urethra and vaginal cystotomy

that a cystotomy is inadvisable. In such cases we resort to a suprapubic drainage tube, also in the form of a mushroom catheter (Fig 11). The vaginal cystotomy closes spontaneously in a remarkably short time after withdrawal of the catheter two weeks later, if the incision has not been made through scar tissue. The suprapubic drainage tract also heals spontaneously within a few days. The patency of the catheters is tested by injecting a few cubic centimeters of normal salt solution daily. With the precaution of double drainage we have never felt it necessary to torture the patient by forcing her to lie in the prone position.

By the application of these principles we have cured 90 per cent of this series of fistulae, many of which had had repeated unsuccessful attempts at closure

#### CONSTRUCTION OF THE DESTROYED OR CONGENITALLY ABSENT URETHRA

Among the most difficult cases of incontinence to cure surgically are those resulting from complete destruction or congenital absence of the urethra,

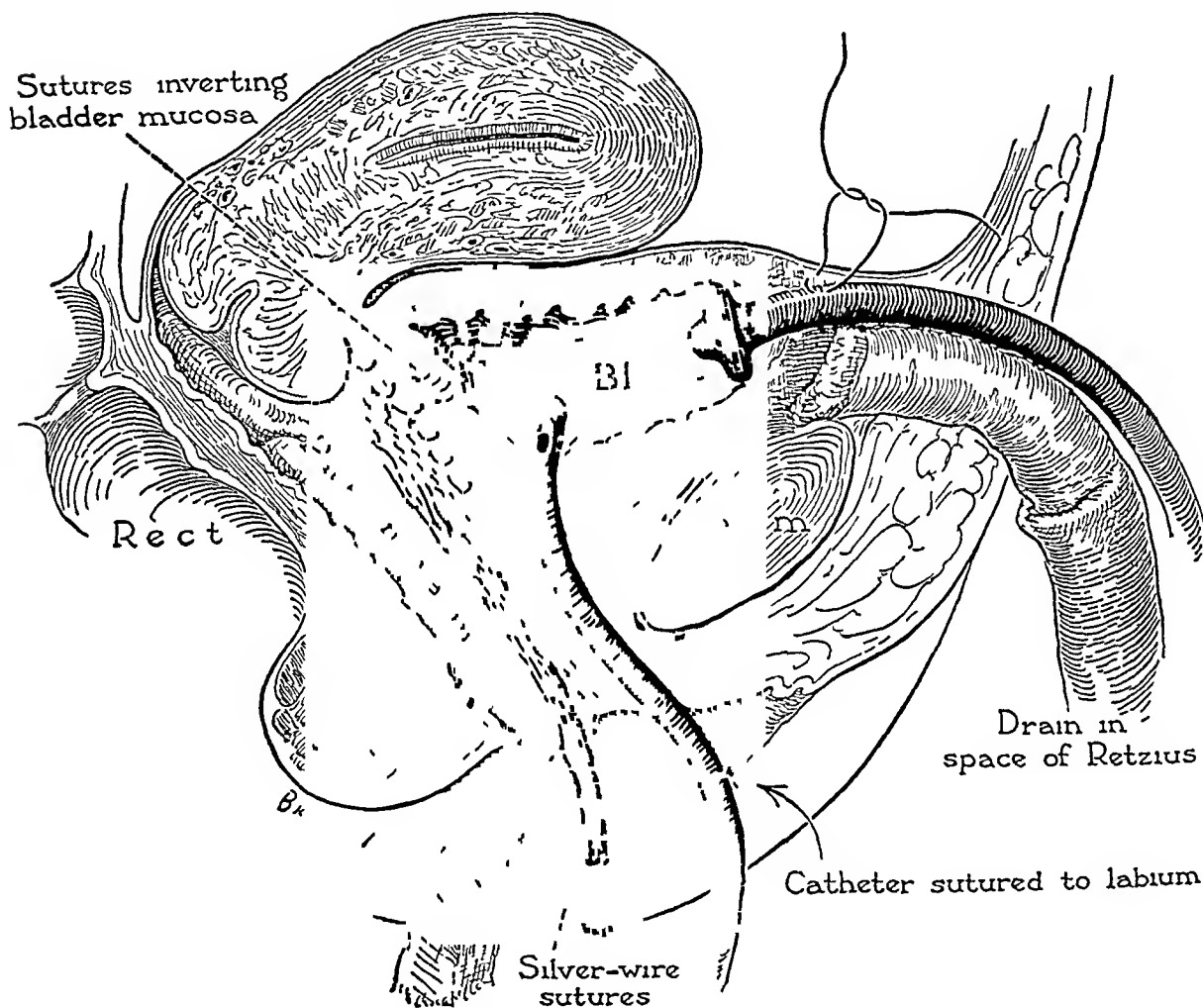


FIG 11—Double bladder drainage through urethra and suprapubic cystotomy

including the region of the internal sphincter. Occasionally, one encounters such a condition as a result of childbirth injury and we have even seen one case in which the entire urethra was cut away by an operator in attempting to repair a cystocele. However, the majority of such cases seen in our clinic are the result of destruction of the urethra by lymphopathia venereum. Such lesions, at times, heal spontaneously, leaving the patient without a urethra but the tissues are left in a state of chronic edema and fibrosis. The tissues are

difficult to work on surgically, which adds to the already difficult task of performing plastic surgery in a field in which a certain amount of infection is inevitable

Many operations have been devised for the formation of a urethra and the existing conditions in the urethral region suggest the best procedure to the operator. Regardless of his choice, failures in restoring continence will be frequent, for even though a perfect mucosal tube is formed, the sphincter is often still deficient.

The operation described here was conceived more or less independently by Drs E H Richardson, Houston Everett, and the author, and we have used it with some success, but also with some failures. It is well suited to a case such as is illustrated in Figure 12.

A U-shaped flap of vaginal mucosa is dissected free, as shown in Figure 12 A, B. When held forward, the under surface of the trigone and sphincter region of the bladder is exposed. The sphincter is tightened by using a few interrupted sutures of medium silk (Fig 12 B). In Figure 12 C, these silk sutures have been tied and the tissue inverted. The flap of mucosa is drawn downward and an area about 6 or 7 mm in width is denuded forward on either side for a distance equal to the length of the flap (Fig 12 D).

The edge of the flap is held forward with a smooth dissecting forceps and curled under, so that the raw surface of the flap may be sutured to the anterior denuded area (Fig 12 E). Interrupted sutures of No 00 chromic catgut are used. This is repeated on the other side, thus, forming an epithelial-lined tube to serve as a urethra.

The wound is closed by approximating the mucosal edges with interrupted sutures of No 0 chromic catgut (Fig 12 F). This buries the newly constructed urethra and closes the wound. The bladder is kept empty by means of a catheter in a surgically made vesicovaginal fistula, placed posterior to the newly made urethra.

#### URETEROVAGINAL FISTULA

Incontinence of urine due to ureterovaginal fistula usually results from operative injury to the ureter. When the ureter is transected but not ligated and the injury unrecognized at the operating table, urine may appear in the vagina almost immediately following the operation. More often the lower ureter sloughs as a result of accidental crushing or interference with its blood supply as in a Wertheim operation for cervical cancer. Then urine appears in the vagina several days after the hysterectomy. The question immediately arises as to whether one is dealing with a vesicovaginal or ureterovaginal fistula. The answer is easily obtained by filling the bladder with methylene blue solution. If the vaginal urine is unstained it is obvious that it is the ureter which communicates with the vagina. Cystoscopic observation of the ureteral orifices will readily prove which ureter has been injured. A ureteral catheter passed up the nonspurting ureter will meet an obstruction, indicating the site of the injury.



One next proceeds to determine the function of each kidney. A differential phthalein test is done by collecting from the uninjured side transvesically through a urethral catheter and collecting from the injured side in a bed pan. Intravenous urograms should be made on discovery of the fistula to determine the status of the upper segment of the injured ureter, the kidney pelvis and calices. Sooner or later these structures will show dilatation as scar tissue contracts about the injury in the ureter and if the condition is neglected kidney function will suffer.

A cure of the incontinence can be effected by nephrectomy, but nephrectomy is an admission of defeat and one's plan should be to save the kidney by performing an anastomosis between the segments of the ureter or the upper segment of the ureter and the bladder. Choosing the optimum time for this surgery is a matter of the keenest surgical judgment. If the operation is undertaken too soon, the pelvic tissues in the region of the ureter will be edematous, and the delicate surgery will be extremely difficult. If, on the other hand, one waits too long the function of the kidney will be reduced or even completely destroyed. The urge to operate within a week or two after the original operation is often irresistible to the surgeon who is responsible for the fistula, but failure is the usual outcome of such early attempts. It is desirable to allow as much as six weeks to elapse before undertaking the anastomosis. However, circumstances sometimes force the surgeon to operate before this time. As one awaits the passage of the six weeks, scar tissue forms about the injured ureter and its contraction may interfere with drainage, resulting in back pressure on the ureter, kidney, pelvis and calices. Slowly, but surely, this will destroy the kidney function. The sudden cessation of vaginal drainage usually is an indication for not too much delay in the contemplated anastomosis. The effect on the kidney should be watched by taking intravenous urograms at frequent intervals. Pyelitis may occur as a result of faulty drainage. This may be an indication for immediate surgery, but if it occurs shortly after the original operation, a temporary nephrostomy may be advisable which is permitted to function while one is waiting for the tissues in the operative field to get into condition for further surgery. If operation upon the ureter must be undertaken in the presence of infected urine, postoperative medication with sulfonamides and penicillin should be carried out.

Upon undertaking the anastomosis one must decide at the operation whether uretero-ureteral or ureterovesical anastomosis is the procedure of choice. In general, ureterovesical anastomosis is an easier procedure, and the chances of success are greater, but the high position of the injury may make it impossible to draw the ureter down to the bladder without excessive ten-

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FIG 12—A A "U"-shaped incision is made through the vaginal mucosa

B Mucosal flap has been freed and pulled forward. Three interrupted sutures of medium silk are placed to tighten sphincter region

C Sphincter sutures have been tied, inverting tissue

D Mucosal flap has been pulled downward and areas denuded anteriorly on both sides

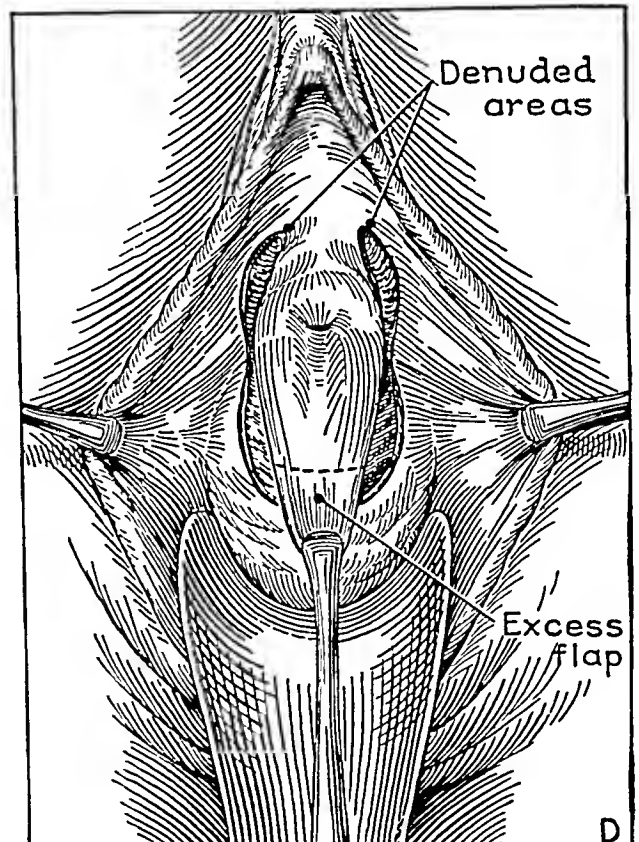
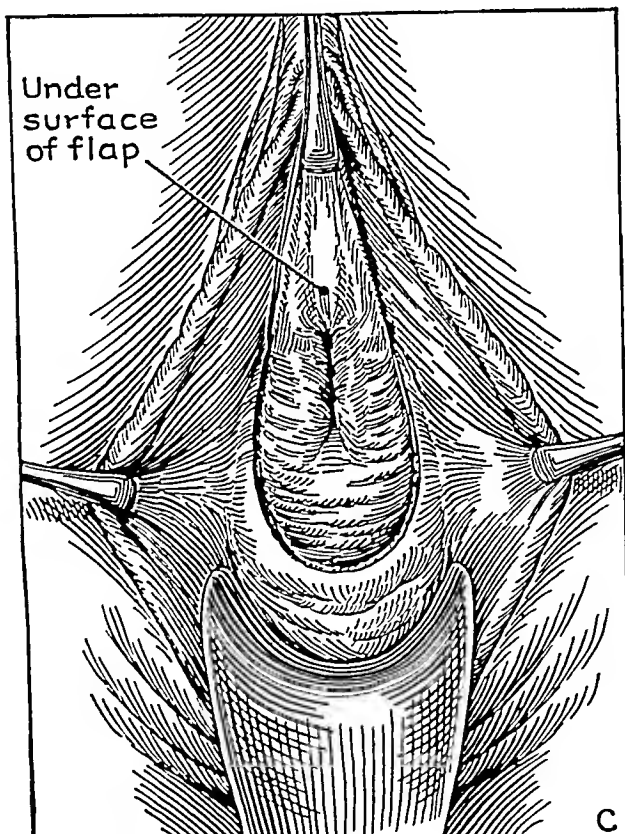
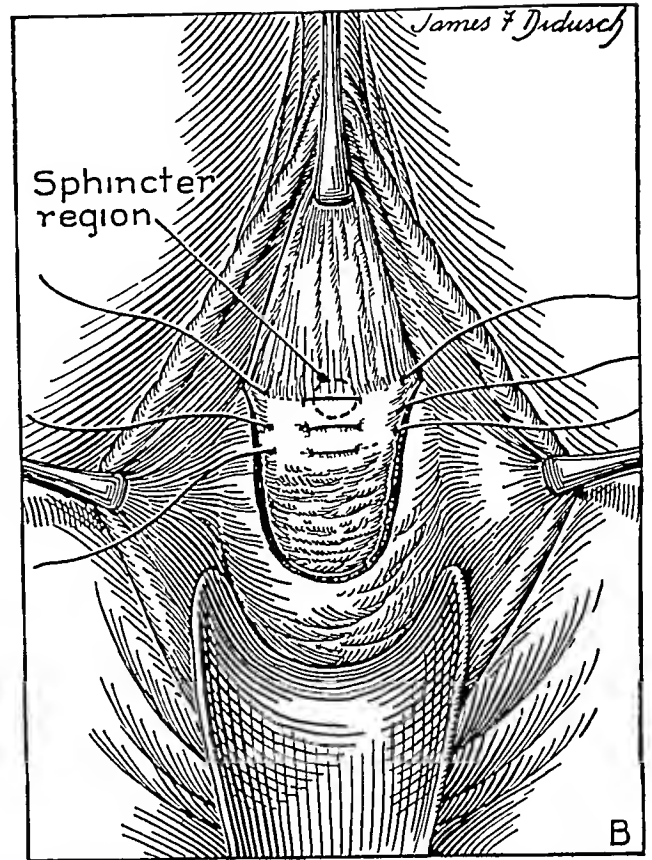
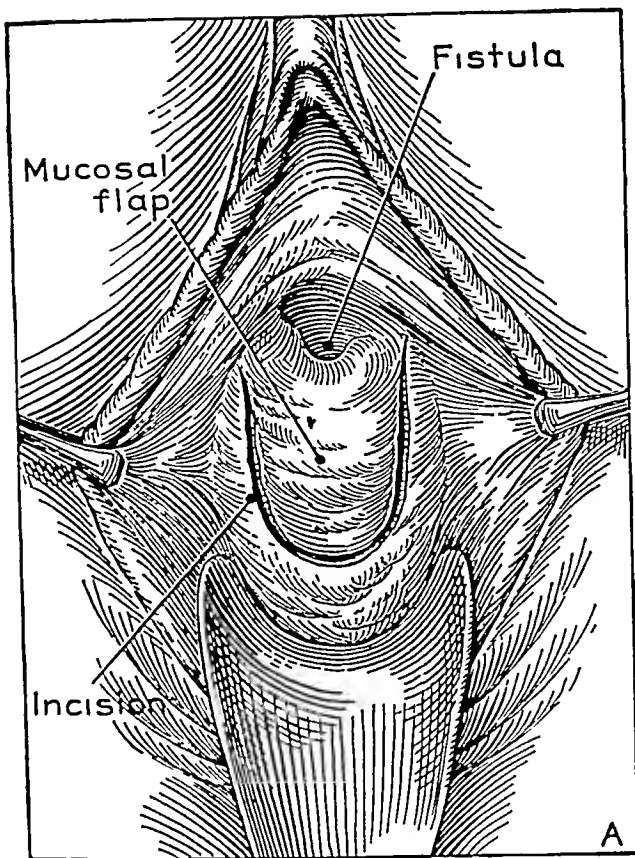


FIG 12  
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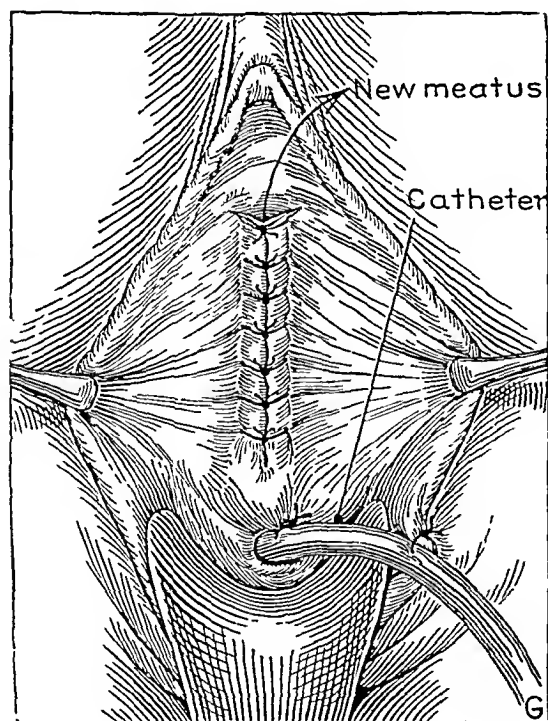
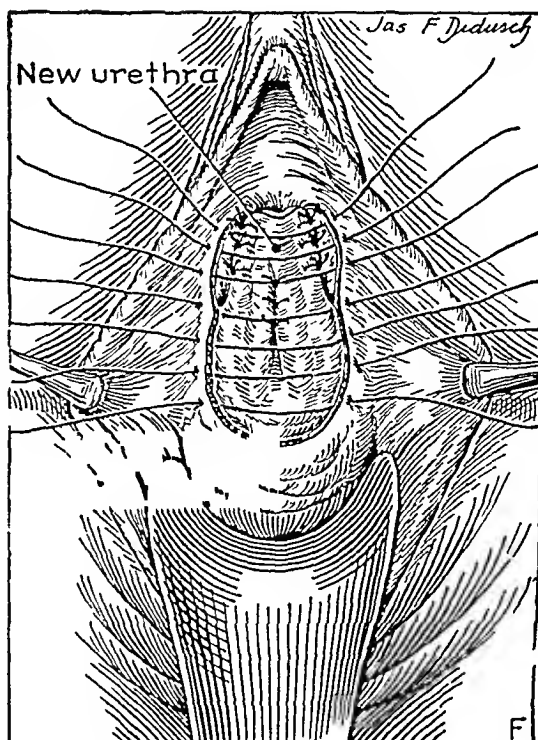
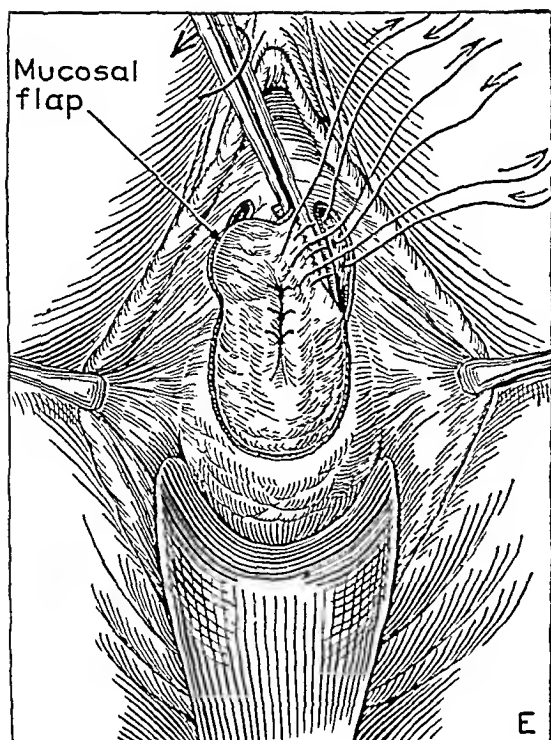


FIG 12—E Flap is sutured anteriorly with No 00 chromic catgut, rolling flap inward so as to approximate raw surface to raw surface

F Mucosal edges are approximated over the newly formed urethra with interrupted sutures of No 0 chromic catgut

G Bladder is kept empty by means of a catheter in a surgically made vesicovaginal fistula placed posterior to plastic work

sion Often, however, it is possible to bring the bladder up to the severed ureter for a considerable distance We have noted no advantage in attempting to perform the anastomosis retroperitoneally

Just before operation the patient should be cystoscoped and a ureteral catheter passed as far as possible up the lower segment of the injured ureter This enables the operator to identify the lower portion of the ureter easily Without this precaution the lower segment, buried in the edematous tissues, may be located only with great difficulty If uretero-ureteral anastomosis is done, the catheter can be pulled up and used as a splint for the anastomosis The anastomosis is done in an end-to-end manner suturing the ureteral walls together loosely with No 000 chromic catgut (Fig 13) The catheter is left in the ureter for approximately ten days During this time the patient is given chemotherapy prophylactically, fluids are forced and the catheter is inspected frequently to be certain that the lumen is patent If it becomes obstructed, it should be irrigated, using a few cubic centimeters of sterile saline solution in a syringe

In performing an implantation of the ureter into the bladder, the ureter is dissected free for a sufficient distance to permit its implantation Excessive freeing of the ureter only strips it of blood supply and increases the danger of sloughing Since most ureteral injuries occur during panhysterectomy, the uterus is out of the way and the ureter can be brought directly down to the

vertex of the bladder If the uterus has not been removed, the shortest path to the bladder is through a perforation in the broad ligament (Fig 14) The lower end of the ureter is split for about 5 mm and a substantial bite is taken into each part of the divided end, using No 00 catgut The vertex of the bladder is held with mucosa clips and a short incision made in it The catheter, which had previously been inserted through the cystoscope up the lower

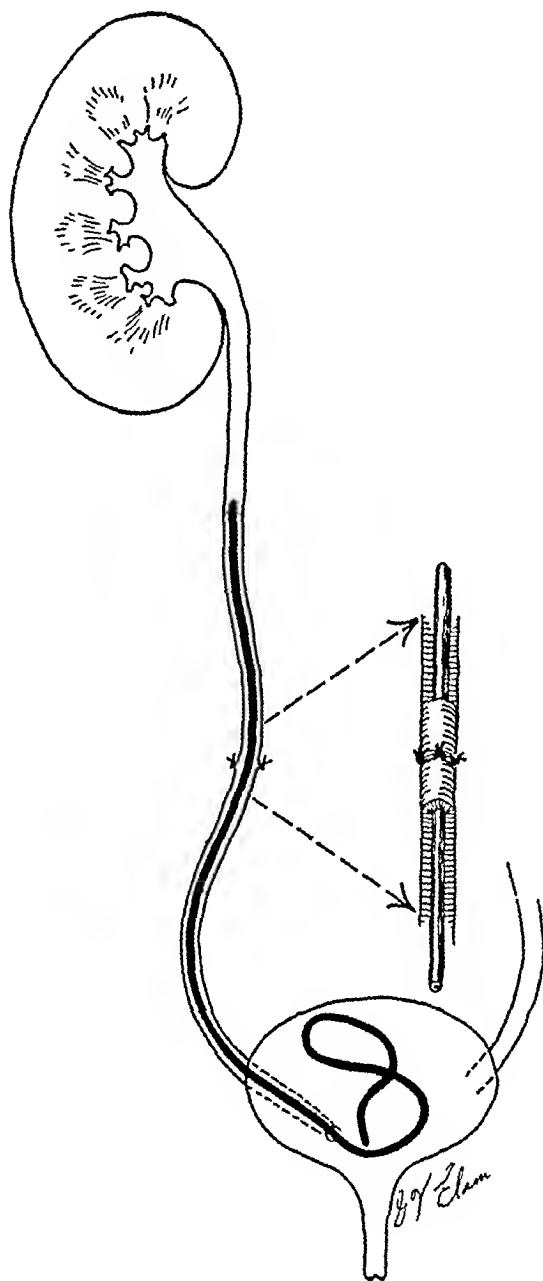


FIG 13 — Uretero-ureteral anastomosis around ureteral catheter

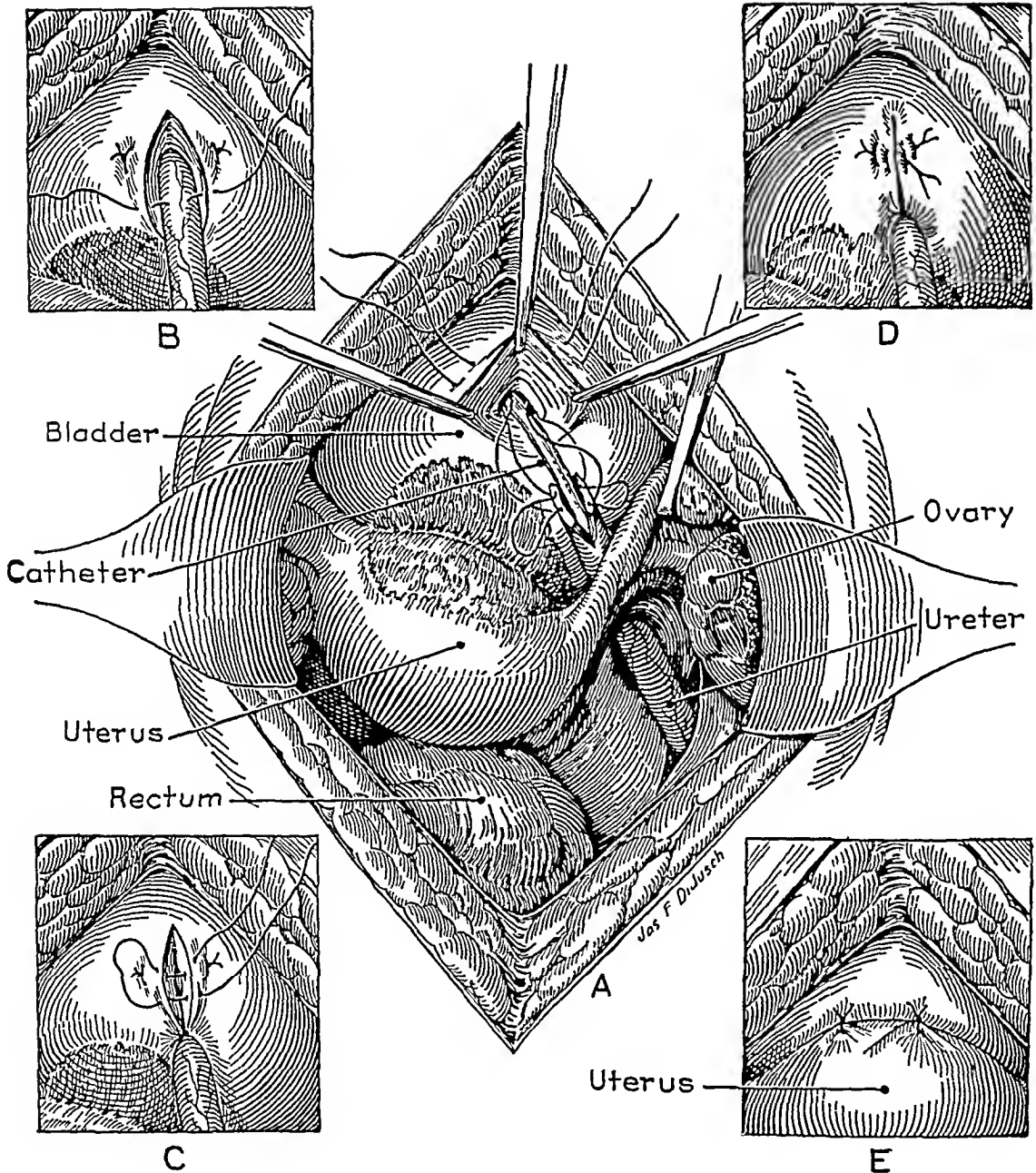


FIG 14—Implantation of ureter into bladder

A Ureter has been dissected free and cut across. Opening has been made through broad ligament into bladder, and end of catheter has been introduced into it. Mattress sutures have been placed in end of ureter, passed into bladder and cut through wall of bladder.

B Mattress sutures have been tied and a fixation suture placed through bladder wall and muscular coat of ureter.

C Bladder-wall incision is approximated with a mattress stitch.

D This mattress stitch has been tied, and implantation has been completed.

E Uterus and serosal surface of bladder are sutured together to relieve any tension that might develop at anastomosis.

segment of the severed ureter, is picked up in the bladder and the end withdrawn through the bladder opening. It is threaded up the ureter which is to be implanted for several centimeters. The four ends of the two sutures which were previously placed in the end of the ureter are then rethreaded on round needles and carried into the bladder and then out on opposite sides of the bladder incision (Fig 14 A). These sutures are tied as shown in Figure 14 B.

A third stitch is taken to fix the ureter to the bladder wall (Fig 14 B). A mattress suture, or two, are used to complete the closure of the bladder wall. If there is tension an attempt should be made to relieve it by fixing the bladder in a high position. If the anastomosis has been satisfactory, 5 Gm of sulfanilamide powder is dusted into the operative field and the abdomen closed without drainage. If there is doubt about the quality of the anastomosis, a cigarette drain should be placed down to the operative region and brought out retroperitoneally through a small stab wound. As in uretero-ureteral anastomosis, the ureteral catheter is left in place for about ten days. A rubber urethral catheter is also left in the bladder and the catheters watched to make certain they are patent at all times. Chemotherapy is administered during the convalescence.

From reviewing our experience of the past decade, it is apparent that most cases of urinary incontinence are curable surgically. In order to effect a cure in a high percentage of cases, surgical principles which have evolved out of the experience of many operators during several decades must be heeded. Ingenuity in planning each case and meticulous care in executing the surgical procedures are essential, but the reward is a successful outcome, which transforms the life of the patient from an almost unbearable existence to that of a normal woman.

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DISCUSSION—DR EDWARD H RICHARDSON, Baltimore, Md This exceptionally clear and comprehensive presentation by Doctor Te Linde leaves little to be added to the subject. Certainly, he is to be congratulated upon the high percentage of success he has obtained, especially in his management of the more difficult types of fistulae.

Of the many valuable lessons contained in this paper, time will permit me to focus attention upon only a few. First, the lamentable fact that the altogether unwise and inaccurate propaganda of recent years, advocating routine total hysterectomy for benign disease, has obviously led many surgeons who are inadequately trained to undertake this operation, with the inevitable result that postoperative urinary tract fistulae are multiplying all over the country at an incalculable rate. This, too, in spite of the fact that several operative procedures have been devised that, if accurately imitated, would certainly reduce the incidence of this distressing sequela to a minimum. In 1929, after an intensive study of the anatomy involved, I published my technic for abdominal total hysterectomy, which is reproduced in Doctor Te Linde's recently published "Operative Gynecology." One of the main objectives in designing that operation was to avoid urinary tract fistulae, and if the technic described is rigidly adhered to, none should occur, as witness the fact that in my own series of cases since 1929 I have not had a single postoperative fistula develop.

Secondly, we have been shown that there is no single operative procedure that can be successfully applied to all types of urinary incontinence. Each patient must first be comprehensively studied and all therapeutic factors marshaled for surgical attack that can in any way contribute to a successful operation. Obviously, this program must include a thorough preliminary general diagnostic study with therapy directed to attainment of the best possible physical and mental condition of the individual patient, it must include specifically an expert urologic study, it must take care that the tissues to be utilized for plastic repair are in suitable condition, that is, free from infection, edema and impaired circulation. All these factors may contribute to defeat if sufficient time, often a matter of six months, or more, is not allowed to elapse for tissue recovery subsequent to the original trauma or to repeated unskilled attempts at reconstruction.

Thirdly, we have been reminded of certain aids, the intelligent use of which often greatly simplifies the plastic procedure. Included among these are (1) optimum exposure, to be obtained by choice of posture (the dorsal posture with elevation of the hips, the Sims posture or, occasionally, the knee-chest posture), by utilizing episiotomy or Schuchardt's pararectal incisions, and by the use of properly placed traction sutures, (2) indwelling catheters in the ureters to avoid occlusion by sutures, (3) the combined extraperitoneal abdominal and vaginal approach when essential to success, and (4) delicately constructed instruments specifically designed for this work.

Finally, emphasis has properly been placed upon strict observance of the fundamental principles of plastic surgery, namely, (1) free mobilization of the margins of the fistula by liberal dissection of the vaginal wall from the bladder on all sides, (2) excision of scar tissue along the margins to a vascular base, (3) judicious hemostasis, (4) accurate approximation of the margins, with an adequate zone of adjacent bladder wall, (5) avoid inclusion of bladder mucosa between the approximated margins, (6) avoid excessive use of sutures lest ischemic necrosis result, (7) avoid a vertically superimposed suture line in closing the vaginal wall and use fine silver wire for the latter, so placed as to obliterate all dead spaces but not penetrate the bladder mucosa, (8) the use of a therapeutic secondary fistula, either vesicovaginal or suprapubic, as may be indicated, with an indwelling catheter to keep the bladder at rest for 12 to 14 days, and (9) meticulous postoperative supervision.

These are the guiding principles in the successful management of urinary incontinence in women, and I am sure that all of us will agree that Doctor Te Linde's slides, together with his discussion of the subject and his excellent statistics, prove quite conclusively that not only is he quite familiar with all of them but also that he possesses uncommon skill and resourcefulness in their practical application.

DR CURTIS H. TYRONE, New Orleans, La. We are indebted to Doctor Te Linde for his very excellent portrayal of this subject, and to Doctor Richardson for his comment. I can certainly agree with him that the number of fistulae from hysterectomy is increasing, and in the last ten years I have seen only one case in which the fistula was due to obstetrical injuries.

Doctor Te Linde stressed the use of silver wire in the correction of vesicovaginal fistulae. I was "raised" on silver wire, but in the last few years I have become converted to cotton. The use of cotton after the bladder mucosa has been closed has worked very successfully in the last few years. I think one most important point in closure is thorough mobilization of the bladder mucous membrane.



# GANGRENE (NONINFECTIVE) COMPLICATING FRACTURES\*

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LITERATURE ON FRACTURES as well as on circulatory disturbances is extensive. Published observations on soft tissue and vascular damage associated with fractures are comparatively rare.

Since soft tissue injuries are extremely common, this represents somewhat of a paradox. Even though the majority of fractures do not present gross evidence of soft tissue injury, it is inconceivable that some damage has not occurred. Fortunately, most of this ultimately proves to be of relative unimportance. However, is it not possible that in emphasizing the treatment of the tangible—the fracture—we have, to a certain extent, minimized the implications of that which is often intangible, *e g*, soft tissue injury? Fractures are often the sequela to an injury which, of itself, monopolizes all attention, and anything else appears to be of relative unimportance. Perhaps it would be a better policy to emphasize and discuss more frequently the potential complications of fractures. Certainly, we should not act as though they were nonexistent. By adoption of such an attitude, adeptness would be gained in treating the usual, as well as anticipating the unusual. Assuredly, anticipation of the possibility of vascular complications would often prevent the development of gangrene, and subsequent loss of an extremity.

In the concept of treatment of fractures, the edict of "splint them where they lie" cannot be overemphasized. However, once beyond that point, a too unimaginative attitude toward proper alignment and fixation of a fracture is frequently revealed, with consequent failure to properly focus attention on possible soft tissue complications, particularly those of vascular or neurogenic character. Once proper immobilization of a fracture has been obtained, it would be wiser to thoroughly evaluate the influence of original trauma rather than attempt to differentiate the possible contributing effects of manipulative procedures. In 1934, Dodd compiled 29 cases of vascular injury complicating fractures of the extremities from world literature and reported two additional cases. The report covered a period from 1850 to 1934. From 1934 to 1942, nine additional cases were reported. Child, in 1942, in reporting a case, reviewed the problem in its relationship to the lower extremity. These two reports represent a recompilation of the 40 cases appearing in world literature from 1850 to 1942.

King and Brewer, in 1944, reported four cases, associated with fractures about the knee, all of which required amputation. They believe that the site of the fracture, rather than the displacement was the important causative

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factor In that same year, Mock and Tannehill reported two cases of gangrene of the lower extremity associated with fractures of the pelvis.

Considering the high incidence of fractures, the condition is apparently strikingly rare Ormsby, in 1911, made the following pertinent observation "The complication of gangrene is an uncommon one if I am to judge from the meager reference to it to be found in the literature at my command "

It is the purpose of this paper to report three additional cases The first two cases, those of popliteal thromboses, came under personal observation The third case, that of a torn brachial artery, was obtained from the University Hospital case reports The interest in each patient is not in the fracture, *per se* but in the complication Therefore, only cursory mention of the type and character of fracture will be made In each instance, contradictory as it may seem, subsequent events proved that the fracture was of minor consequence when compared to the degree of vascular damage All three cases developed extensive gangrene as the result of vascular injury associated with fractures Amputation was required in each instance Each patient recovered

#### CASE REPORTS

Case 1—White, male, age 28, was admitted to the hospital approximately two hours after having fallen 30 feet Injuries were sustained to both lower extremities, resulting in comminuted fractures of the lower third of the right tibia and fibula, as well as the upper third of the left tibia, and the lateral condyle of the left tibia and left patella

When admitted to the hospital, both lower extremities were immobilized in Thomas leg splints The toes were normal in color and sensation intact No evidence of soft tissue damage was noted except for multiple contusions Peripheral vessels were not palpated for pulsations

Under sodium pentothal anesthesia, the fractures were reduced on the day of admission Two attempts were made before the lateral condyle of the left tibia was considered to be in satisfactory position Both lower extremities were encased in plaster

During the next two days nothing unusual was noted, except for the development of pain in the left foot and leg that gradually increased in severity On the fifth day after admission, definite evidence of circulatory embarrassment in the left foot was presented The toes were cold and cyanotic Encasement was removed and immobilization maintained by means of sand-bags The left popliteal, dorsalis pedis and posterior tibial arteries were not palpable Despite supportive measures directed toward stimulating the collateral circulation, the involved foot, ankle and lower two-thirds of the leg became gangrenous A supracondylar guillotine-type of amputation was performed, ten days after the initial injury

Recovery was without event

Subsequent pathologic examination revealed a thrombosis of the popliteal artery at its bifurcation

Case 2—White, male, age 23, incurred a transverse fracture of the left femur with moderate displacement at the junction of its lower and middle third There was no visible evidence of soft tissue damage and notation was not made of associated vascular or neurogenic injury

An immediate reduction of the fracture was performed under sodium pentothal anesthesia and immobilization maintained by encasement in a plaster cast Upon recovery from anesthesia, complaint was made of excruciating pain It was noted that the toes were discolored and cool The encasement, which was relatively loose-fitting, was not considered a contributing factor, and, therefore, was neither removed nor bivalved

When seen in consultation on the third day after the accident, the toes and foot were deeply cyanotic. The encasement was removed. The entire leg was cold and mottled. No pulsations were obtained in the popliteal, dorsalis pedis or posterior tibial arteries of the involved extremity. Supportive measures which were directed toward stimulating the collateral circulation were inadequate. Gangrene developed, and on the tenth day after the initial injury, an amputation was performed at the fracture site.

Subsequent pathologic examination revealed an organizing thrombus of the popliteal artery at its bifurcation, with complete occlusion of the lumen. The dorsalis pedis artery also presented an organizing thrombus. The muscles of the leg were edematous and under considerable pressure within their fascial sheath.

**COMMENT** Supportive measures in Cases 1 and 2 consisted of the use of intravenous papaverine hydrochloride, heparin and paravertebral sympathetic blocks.

No attempt was made to localize the thrombus. No part of the vascular trunk was explored.

A fasciotomy, if it had been performed in Case 2, might have been of value.

**Case 3**—White, male, age 57, fell from a scaffold and incurred a posterior displacement of the right elbow and a comminuted impacted fracture of the distal end of the right radius.

The family physician, after reducing the dislocation and attempting to reduce the fracture, placed the arm and forearm in a plaster encasement. Forty-eight hours later, it was noted that the right hand was cold and painful. During the next 24 hours discoloration of the fingers was observed. The encasement was removed from the arm and elbow region.

Discoloration increased, and three days later, or six days after the initial injury, the remainder of the encasement was removed, at which time a dry gangrene of the forearm was noted. Two days later, when an amputation was performed through the lower end of the arm, the gangrenous process included the entire hand and forearm to within about three inches of the elbow.

Subsequent pathologic examination revealed a tear in the brachial artery that included about two-thirds of its circumference. There was an extensive hematoma in the antecubital fossa and extravasation of blood along the artery. A thrombus occluded the distal part of the brachial artery and extended the entire length of both the radial and ulna arteries. Blood vessel walls were within histologically normal limitations for an individual this age.

**COMMENT** These three cases, although representing a comparatively rare entity, are presented for critical review because of their importance. Proper anticipation, early diagnosis and adequate evaluation of this type of complication are the important factors in preventing the catastrophe of gangrene. Appreciation of the possible implications of trauma to the vascular system should lead to more satisfactory end-results.

**Age Incidence**—Child, in his critical analysis of 15 cases demonstrated an average age of 26 years. He thought that degenerative diseases of the arterial wall, as a predisposing factor, could largely be discounted.

Dodd mentioned calcification of arteries, syphilis and diabetes as predisposing factors.

The average age for the two cases of thrombosis herein described was

25 5 years No evidence of arterial degenerative disease was noted in any of the three cases in this series

*Artery Occluded*—In vascular occlusions there is a direct relationship between the character and importance of the involved artery and the degree of circulatory embarrassment In this series, two cases showed an occlusion of the popliteal artery at its bifurcation The third case presented an interruption to the continuity of the brachial artery by partial severance near its bifurcation Dodd indicated that in association with extremity fractures, the femoral, popliteal and brachial arteries are more susceptible to injury than other peripheral vessels He believes that the explanation for this predilection is the relative greater fixation of these vessels A relatively mobile vessel will be less apt to be involved in accidents, than one more fixed by fascia, aponeurosis or other anatomical factors or in close proximity to bone

In his survey of the subject, Dodd points in particular to the vulnerability of the popliteal artery at its bifurcation and states "This is anchored by the fibrous arch of the soleus, by the passage of the anterior tibial artery over the interosseous membrane, by its proximity to the fibula and by the origins of small anastomotic branches of the knee joint" He, furthermore, discusses the comparatively intimate association of the bifurcation with the neck of the fibula, and points out that the anterior tibial artery makes a slight groove on the inside of the neck of the fibula as it passes from behind to the front compartment of the leg

*Site and Extent of Fracture*—This is apparently not a predisposing factor except in its anatomic relationship to the involved artery

*Method of Treatment of Fracture*—Although it is impossible to refute indictment of encasement, particularly in Cases 1 and 2, it is probable that this method of immobilization was not related to the complication Child, in analyzing 13 cases, noted that six had been treated by traction, five with encasements, and two without either of these aids to fixation

*Results*—In the three cases herein reported, amputation was required There were no deaths Dodd, in his analysis of 31 cases, reported amputations in all but four cases Previous to 1918, the mortality rate was strikingly high The lowered mortality rate since 1918 is attributed to refinements in aseptic technic, rather than operative improvements

*DISCUSSION*—Interruption of blood supply, with inability to establish compensatory collateral flow, will result in death of tissue

Interruption of blood supply may be produced by penetration, complete division or partial rupture of an artery Intimal damage either by contusion, rupture or persistent pressure effect will result in occlusion of the vessel with thrombus formation Leriche believes that thrombosis of an artery or vein is probably the most frequent cause of vasoconstriction and associated spasm He states that as soon as the inflammatory process in its wall reaches the nervous elements of the latter, it stimulates them and this stimulation produces a distal vasoconstriction in the still permeable portion of the artery and over the whole collateral network Excision of the obliterated segment results in a much more active collateral network Conversely, segmental spasm—

*"stupeur arterielle"*—may be due to direct stimulus and if allowed to persist for any great length of time may lead to thrombus development. It is possible that the latter phenomena is a major contributing factor in the production of this condition. The sympathetic responds to all stimuli by a hyper-tonus which lessens the arterial caliber of normal tonus. Simple manipulations and handling of blood vessels will often produce prolonged spasm. It is a condition that is frequently seen in operative procedures. Where there has been trauma or violence of any character, every attempt should be made to evaluate the resultant extent of soft tissue injury, especially in its relationship to vasospasm and vascular interference.

Prolonged pressure effects from edema, tense fascial planes and encasement under certain conditions may be indicting factors in the production of arterial occlusion.

#### TREATMENT

Treatment is a matter of early diagnosis and timely decision. Inevitably, gangrene requires amputation. To avoid amputation, gangrene must be prevented, to prevent gangrene, the circulation must be adequate, and to maintain an adequate circulation, it must be anticipated that it is possible for it either to be, or to become inadequate. This can only be accomplished by individual evaluation of all factors concerned.

If evidence of circulatory embarrassment is discerned and it is believed that bone fragment displacement is not the causative factor, then preferably, the vascular system should be supported, before manipulation for perfect apposition is attempted. If, in every case of fracture, the possibility of gangrene were anticipated, this complication might be averted. Particularly, emphasis should be placed on an evaluation of the status of the peripheral circulation. Failing or absent arterial pulsation, loss of sensation, coldness, cyanosis and pain should be evaluated as being prognostic of imminent circulatory embarrassment. Once suspected, definite and immediate measures should be adopted to support the circulation.

Paravertebral blocks for the dual purpose of overcoming associated spasm and dilating the collateral blood vessels should be effected. Hepatinization, if thrombosis is suspected, should be instituted. The peripheral circulation should be supported by the use of antispasmodics, such as papaverine hydrochloride and liberal sedation. Lowering the metabolic demands by wrapping the extremity in gauze kept moistened with alcohol, as a modified form of refrigeration, will occasionally be found to be of value.

Large hematomas should be incised both to relieve pressure and explore for an injured vessel. When possible, damaged vessels should be repaired either by suture or free venous graft.

Analysis of the cases on record indicates that usually some warning of the imminence of this type complication is given. Careful evaluation and appreciation of the requirements for maintenance of tissue viability may result in the avoidance of this catastrophe.

SUMMARY

The problem of noninfective gangrene following fracture is reviewed.

Three additional cases are recorded

Factors in diagnosis are discussed in addition to therapeutic measures

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DISCUSSION—DR FREDERICK A BOTHE, Philadelphia, Pa I hesitate very much to speak of one case, however, I wish to present the case of a boy, age 17, who received a fracture of both bones of the right leg in a football game The bones were in excellent position There was very little swelling of the leg when he was seen a few hours after the injury The pulsation of the large vessels distal to the site of injury was not determined The fragments were molded into position and a plaster encasement was applied The patient was seen 24, 48, and 96 hours after the application of the encasement The foot was warm, normal in color, and there was no swelling On the 7th day, while attending a football game, he was jostled in the crowd and again injured the same extremity That evening there was some tingling in the knee, the next day the toes were swollen and cyanotic, and tactile sense was gone He then returned for an examination In view of the above findings the encasement was removed at once and the foot elevated There was improvement in the local findings, but not so much as we desired We were unable to palpate any pulsation of either the posterior tibial or dorsalis pedis arteries At this time, tactile sense was absent to the middle of the calf We packed the foot and leg in ice and used repeated sympathetic blocks, but were discouraged by the response to this form of treatment

Dr M C Peterson, of New York, suggested the use of novocaine intravenously instead of the sympathetic block We prepared a solution in which 1 Gm of novocaine was dissolved in 1,000 cc of normal saline Three hundred cubic centimeters of this solution was administered intravenously every eight hours, with a surgical resident in attendance We felt that an equal and possibly greater response occurred from this procedure than from the sympathetic block, and, surely, it is much more easily administered After 48 hours of this treatment we could get a pulsation of the posterior tibial

artery The refrigeration was omitted from time-to-time for a few hours to note any local change At the end of the 4th day the refrigeration was discontinued as we no longer noted any local change when we omitted it for several hours Now, 11 days since we started intravenous novocaine, the phalanges of four toes are gangrenous but the rest of the foot appears improved

This case is presented, not because of the result obtained, but to report the use of novocaine intravenously in the management of cases of peripheral vascular disease Peterson is studying its use in such cases

DR JAMES S SPILL, Memphis, Tenn Doctor Yeager's paper is of great interest and importance to those who engage in the treatment of fractures and other traumatic injuries It calls our attention to the importance of a careful record on these injuries regarding the possible vascular and neurologic damage at the time of the original examination This is of importance, not only in the treatment of the patient but from a medicolegal standpoint as well Vascular and neurologic injuries of this type usually occur in association with fractures at two sites fractures about the elbow joint, and fractures or epiphyseal separations about the upper end of the tibia or lower end of the femur The adjacent vessels and nerves are frequently injured at these sites

The two direct surgical attacks to improve the circulation at the time of the acute injury, embolectomy and spreading of the fascial covering of the muscles about the site of injury, have proved somewhat disappointing in my experience We have found it difficult in most cases to determine at the time of the acute injury whether the vascular damage is temporary or permanent, or whether it is of sufficient severity to jeopardize treatment of the fracture by the institution of such procedures Frequently, by the time a decision has been made in regard to this, the tissue damage due to circulatory disturbance has progressed to a point where these procedures may be of little value

Sympathetic block by any of the accepted procedures has proved to be of considerable help in differentiating between serious permanent vascular lesions and temporary vascular disturbances due to vasospasm Temporary sympathetic block by means of novocaine or alcohol injection is uncertain and transient in its effects

In many cases, where the associated injury has produced serious shock, the addition of any major surgical procedure is inadvisable In these cases continuous caudal anesthesia for vascular disturbance in the lower extremities has been found to be very helpful It has been continued in one of our cases for seven days without any deleterious effects It is possible that, when additional experience and knowledge have been gained in the use of tetra-ethyl-ammonium, that this will prove to be an agent of choice, both as a therapeutic measure and as a diagnostic measure, in many cases

It is important from a medicolegal standpoint to have recorded that vascular disturbances of serious nature may occur in extremities where no type of constricting bandage or immobilization has been used

DR GEORGE E BENNETT, Baltimore, Md From time-to-time one sees a fracture of the lower leg in which there is complete blanching of the tissue below the line of fracture and lack of pulsation of the vessels of the foot After the fracture has been reduced and held in position manually for a period of a few minutes, and blushing of the skin and circulation does not return, then I think one is perfectly justified in dividing the fascia of the calf of the leg to relieve this pressure, just as one would do in the upper arm associated with fractures of the elbow I have done this on many occasions and I feel quite sure that I have saved many patients serious circulatory complications of the leg

DR J M DONALD, Birmingham, Ala I wish to express my appreciation for Doctor Yeager's splendid presentation of this very important subject and to report a somewhat similar case Complete laceration of the popliteal artery following posterior dislocation of the left knee, with resulting gangrene of the leg requiring amputation

**Case Report**—This 27-year-old white male was brought to the Hillman emergency room on the night of January 16, 1946, shortly after an automobile accident near Birmingham. The patient stated that he was a passenger and was asleep in a truck which overturned. He was found thrown from the car and was wedged between the car door and a tree. On admission, the patient was in severe shock. There was pain and swelling about both knee joints. After treatment for shock and application of Thomas leg splints to both lower extremities, he was admitted to the surgical service of the Jefferson Hospital.

About three hours after admission it was noted that the left foot was cold, whereas the right foot was warm. Traction was immediately released from the left leg and ice bags were packed around the leg. No pulsation could be felt in the left dorsalis pedis or posterior tibial arteries. The patient complained of severe pain in the left leg. Left lumbar sympathetic blocks were done without apparent benefit. Roentgenologic examinations revealed no evidence of fracture of the left leg. Roentgenologic examination of the right knee revealed a comminuted fracture of the anterior lip of the right tibial condyles and an incomplete fracture through the head of the right fibula.

After two days of conservative therapy there was no improvement in the circulation of the left leg. The left calf was ecchymotic, edematous and tense. The left foot was cold and blanched. Dr. J. M. Mason III saw the patient in consultation and advised fasciotomy and exploration of the left popliteal space. These procedures were carried out under spinal anesthesia. The left popliteal artery was found to be completely severed just proximal to its bifurcation. The popliteal vein was thrombosed. The ligaments of the knee joint were extensively torn. The severed popliteal artery was extremely spastic and a thrombus was present in each end. Due to the tearing effect of the injury, suture of the artery was impossible. The ends of the artery were ligated. The popliteal wound was closed. After dressing the fasciotomy wounds the leg was well padded and placed in a plaster encasement which was immediately bivalved.

In spite of repeated lumbar sympathetic blocks, gangrene of the foot and leg progressed.

On January 23rd, seven days after injury, amputation of the left leg above the knee was performed under spinal anesthesia. The wound was closed primarily. An encasement was applied to the right leg on January 28th. The patient improved rapidly. Convalescence was uneventful. The patient was discharged from the hospital in good condition on February 10, 1946.

This case serves to emphasize the seriousness of injury to the popliteal artery. It seems probable, since no fracture was demonstrable, that the tearing of the artery was due to dislocation of the knee joint.

DR. J. WARREN WHITE, Greenville, S. C. One point would bear emphasizing, that is, the value of cold. Doctor Yeager mentioned the use of alcohol but not the use of ice and ice packs. I think this is one point that should be considered and would be of real help. In the cases cited probably nothing could have been done. If, in the face of threatened gangrene, you can lower the metabolic requirement you might protect the leg until you get restoration of circulation. Another point deserving emphasis is to elevate the extremity, as I am sure we always do. I use the ice bag postoperatively in all cases, if only for the comfort of the patient.

DR. I. R. TRIMBLE, Baltimore, Md. In these very acute emergencies I would like to make one plea on treatment. A great many of these patients should be subjected immediately to lumbar sympathectomy through the extraperitoneal approach. It is easily done, taking only a few minutes. If the leg is in danger because of poor circulation a real emergency exists, and we should not wait until developments of a serious nature have taken place. If there is no pulsation at the time of injury and examination shows that fasciotomy should be done, well and good. On the other hand, in any injury with spasm of the large vessels there is always great spasm of the accompanying vessels. This can be relieved by sympathectomy. The trouble with injections is that it is not known how long they will last. It is difficult sometimes to turn the patient in bed to subject him to multiple injections. I think instead of continuous spinal anesthesia of a week's duration, short spinal anesthesia and sympathectomy would be more reasonable. Once that is done you know you have given all the supporting measures you can to increase the collateral



circulation in that leg, and I think we are going to find that in the future we shall resort to actual sympathectomy rather than to injections or other measures

DR. GEORGE H YEAGER, Baltimore, Md, (closing) I want to thank all the discussers I have had no experience with intravenous novocaine The recommendation is most pertinent Two of the patients were seen under conditions where ice was not available We are using modified refrigeration where it is possible When ice is not available or advisable, gauze saturated with alcohol over the involved extremity will prove of value I agree with Doctor Trimble that ganglionectomy is the effective method of overcoming vasospasm Unfortunately, the diagnosis is usually made late and not at the time trauma occurs At the time of identification thrombosis has already occurred With evidence of gangrene presenting, it is difficult to rationalize a major operation to prevent a condition that has occurred Possibly, one might be justified in considering excision of vessels or resection This will accomplish much in overcoming vasospasm

## SHOULDER AND ELBOW LESIONS DISTINCTIVE OF BASEBALL PLAYERS\*

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IN A FORMER PUBLICATION<sup>1</sup> I stressed the point that the professional baseball player was a human being, not a superman, and that he was susceptible to all of the common lesions of the shoulder which we see in the non-ball player, namely, subacromion and subdeltoid bursitis, irritation of the supraspinatus and biceps tendons, traumatic synovitis and inflammatory disease. Fortunately, these conditions form the largest group and respond well to rest, heat and general orthodox treatment. Because a man is a ball player does not mean that he cannot have abscessed teeth, infected tonsils, or other foci of infection, therefore, his general health should be thoroughly investigated, just as one does when in search of some obscure etiologic factor in joint lesions.

His occupation is such, however, that aside from these common joint complaints he develops distinctive lesions. One which has been definitely identified and, to my knowledge, is nonexistent in other occupations, is a deposit on the posterior and inferior margin of the glenoid fossa, on or about the attachment of the triceps tendon. This is the result of the abnormal strain which is placed on the shoulder in throwing a baseball. As the arm swings forward in a flail-like movement with complete relaxation of the muscles of the shoulder, which is so essential for a pitcher to be effective, a tremendous strain is thrown upon the posterior shoulder and, as a result, deposits or exostoses develop in close proximity to the circumflex nerve and this nerve becomes irritated and causes marked referred pain to the shoulder joint, particularly in the region of the deltoid muscle. This is one of the distinctive lesions which very often ends the career of a professional pitcher as, in my opinion, it does not respond well to surgery. The cause is abnormal use of the shoulder and the deposits cause no discomfort or inconvenience except when throwing a baseball hard (Fig 1).

The second lesion is a fraying of the supraspinatus tendon, which I do not think we can class as distinctive, because one sees it in individuals engaged in other occupations. The constant snubbing of the supraspinatus tendon over the head of the humerus and the greater tuberosity results in a gradual fraying of the deeper structures of the supraspinatus tendon. This is usually a lesion of a veteran pitcher after many years of professional baseball. On exploring these shoulders the outer surface of the supraspinatus tendon looks perfectly normal but a linear incision in the fibers of the tendon will show fraying of

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A



B

Figs 2A and 2B—Typical small osseous growth in the ligamentous tissue posterior and inferior to the internal epicondyle

A



B



Figs 1A and 1B—Characteristic deposits on the posterior-inferior border of the glenoid

that portion which is in contact with the humerus. Again, I do not think this is a remedial lesion. It is the result of prolonged use and abnormal irritation and does not respond to surgery. It also is a condition which causes no discomfort except when throwing a baseball hard.

The common pathologic processes of the elbow joint in the professional ball player are strikingly similar to those seen in non-ball players—loose bodies, single or multiple, either in the olecranon fossa, about the head of the radius or about the coronoid process. Generalized osteo-arthritis is also seen in non-ball players. There are, however, two lesions of the elbow which I

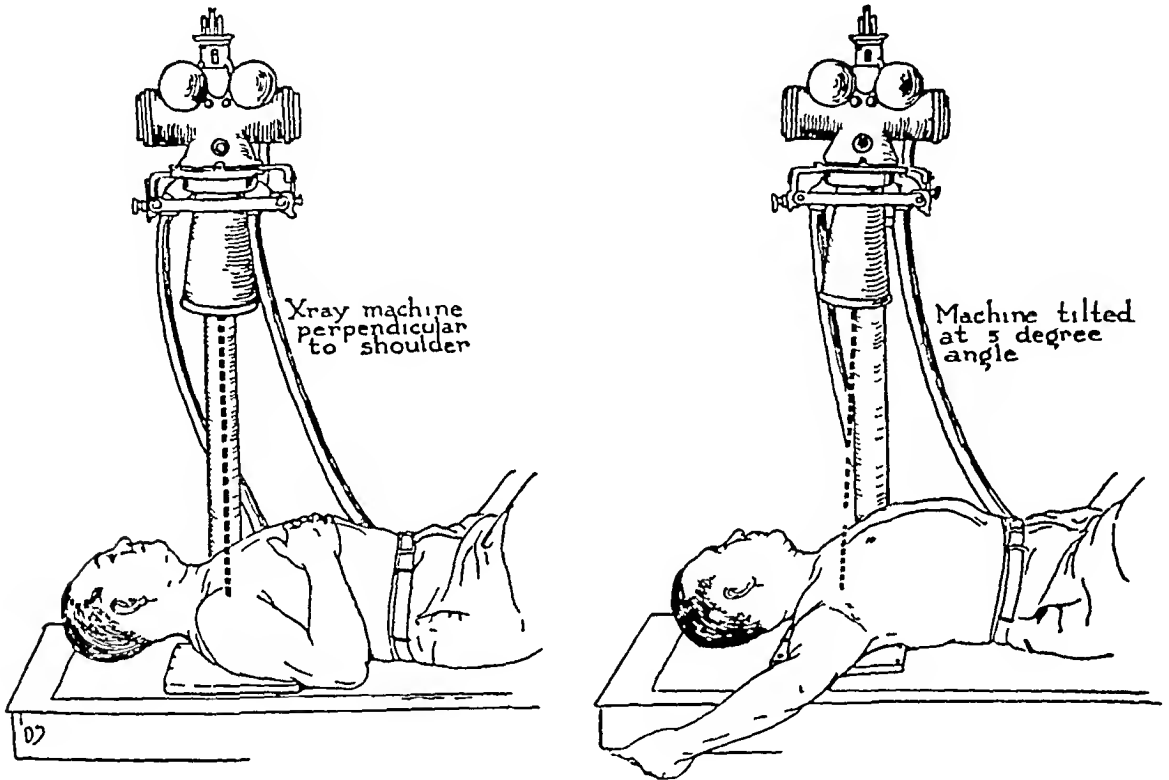


FIG 3—The exostosis or deposit in the posterior inferior region of the glenoid cannot be identified by the ordinary anterior posterior or posterior anterior view of the shoulder. Our x-ray technician, Mr. W. Ross Mitchell, developed the technic shown here. External rotation of the humerus with tilting of the x-ray tube about 5 degrees is the position which rotates the head of the humerus and the glenoid to a position which throws the thickened area in relief. (J. A. M. A., 117: 510-514, 1941)

think are distinctive. A pitcher in throwing a curve ball is compelled to supinate his wrist with a snap at the end of his delivery. This movement plus extension leads to the development of an irritation in front of the internal condyle of the humerus which is extremely disabling and very often ends his career. On examination one will note distinct fullness over the pronator radii teres, beneath which are the tendinous attachments of the brachialis and the flexor sublimis digitorum. These are covered by a very strong fascial band, a portion of which is the attachment of the biceps which runs obliquely across the pronator muscle. A pitcher may be able to pitch for two or three innings when the pain and swelling becomes so great that he has to retire. Roent-

genograms in the majority of cases are entirely negative, and on exploration the joint reveals very little. The muscle tissue generally is normal in appearance. The simple division of the fascia covering the muscles has, on occasions, rehabilitated these men so that they were able to return to the game. I am at a loss to explain it except that tension develops from some unidentified irritation to the muscle tissue which at times has an ischemic appearance. It is quite possible that this may be a secondary irritation which is the result of lipping of the ulna at its articulation with the internal condyle, because on rare occasions we see osteophytic processes here which are linked with the condition which I am endeavoring to describe. I am not clear in my own mind as to its exact pathology. I trust that further study and observation will clear up this point because I feel that it should be a remediable lesion.

The most distinctive lesion, and one which is not seen in other occupations, is the development of single or multiple deposits of bone or ossicles in the ligamentous tissue and tendinous attachments beneath the ulnar nerve and not within the joint. I am quite sure that these deposits are purely the result of chronic strain and probably take years to develop, and in many instances give no symptoms. When they begin to cause irritation of the ulnar nerve they can be removed with success. Identifying these small masses of bone in the ligamentous tissue and dissecting them free will relieve symptoms in most cases.

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# MEMOIRS

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## HOWARD MERRILL CLUTE

1890-1946

DR HOWARD MERRILL CLUTE was born in North Berwick, Maine on January 10, 1890 and died in Boston, September 19, 1946. He was graduated from Dartmouth College in 1911 and from the Dartmouth Medical School in 1914. He received an honorary degree of Doctor of Science from Dartmouth in 1941.

He did his graduate work in surgery at the Boston City Hospital and then entered military service during World War I, receiving the rank of Major upon discharge.

After a long and successful association with Dr. Frank Howard Lahey, he entered private practice in Boston in 1935. One year later, he was made professor of surgery of the Boston University School of Medicine and surgeon-in-chief of the Massachusetts Memorial Hospital. He fulfilled his obligations to these Institutions with unusual and outstanding devotion, and upon his retirement in 1945 he was elected to their Board of Trustees.

Doctor Clute was interested in national and international affairs and through his contributions was made a member of many organizations, whose chief interest was in the advancement of surgery. In addition to the Southern Surgical Society, he was a member of the International Surgical Society, the American Surgical Association, the New England Surgical Society, and the American Society for the Study of Goitre. He was past president of the Boston Surgical Society and chairman of the credentials committee for the State of Massachusetts of the American College of Surgeons. He was a founder member of the American Board of Surgery and served on its examining committee for several years.

Clute was a skillful surgeon, a persistent student, an excellent diagnostician, and an able teacher. He had the rare ability to apply his native talents in a manner that successfully combined his analytical mind, dexterity, and common sense. His patients, his consultants, and his friends admired and adored him.

Howard Clute was known for his interest in humanity. He loved a party and engaged in the usual sports to some extent. His happiest moments outside the operating room were those spent with his cronies. Bridge, perhaps being his chief diversion, with his classmates Ben Ames Williams and Leland Powers, Jr., he spent many happy evenings. These companions of literary and legal fame doubtless tried to keep him from working too hard, but probably in an indirect manner spurred him on to attain a high peak of success in his own field.

His contributions to the surgical literature were numerous. Many of his observations and deductions will live in the minds of students of surgery for decades to come. The practical and useful side to his papers will long be remembered by his colleagues.

Clute died in the harness as he would have wished it. Having performed a successful and difficult operation in the morning, and run off a busy office hour in the afternoon, he went to his home and quietly passed from this world into the next. Those of us who knew him in his last years admired his spirit, his courage, and his determination to carry on in spite of his earlier attacks of coronary thrombosis.

Doctor Clute is survived by his devoted wife, a son Charles, and a daughter Alice. He was a good husband and father. Not only will these members of his family be glad to have known this man but so will his friends and associates remember his fine qualities, his keen wit, and his devotion to the art of surgery.

ARTHUR W. ALLIN, M.D.

## WALTER E DANDY

1886-1946

THE DEATH of Walter E Dandy on Good Friday, 1946, came as a surprise to many people. A few premonitory symptoms of the fatal coronary occlusion had been misinterpreted during his winter vacation in Florida. There had been sufficient anginal pain during the last two weeks of his life to cause him to have electrocardiographic studies, but the final episode came with that stunning suddenness which one sees so often in coronary disease. Doctor Dandy was born in Sedalia, Mo., in April, 1886. He was the only child of parents who had



Walter E Dandy

come from England a few years before he was born. His exceptional mental capacity was recognized early in life, and his fourth-grade teacher, Miss Cousley, encouraged him to do two years work in one year. He led his class on graduation from high school and took his collegiate work at the University of Missouri.

At college Walter Dandy was particularly interested in biology, and became an assistant to Doctor Curtis, the head of that department. It was due to the advice of this teacher that his exceptional pupil entered the Medical School at Johns Hopkins with advanced standing. Here he spent his spare hours doing investigative work in anatomy. Fortunately he was attracted to neurosurgery while a student, and never wavered from his determination to become foremost



in this field. It is not surprising, therefore, that Cushing's refusal to take him to Boston in 1912 was a disappointment that depressed Doctor Dandy for months. Late in life he remarked that Cushing's decision was the best thing that had ever happened to him.

After spending eight years as a house officer, assistant resident and resident in general surgery at the Johns Hopkins Hospital, Doctor Dandy put in one year on a full-time basis, and then went into private practice.

It was during his year as assistant resident (1913) that Dandy and Blackfan worked out the pathogenesis of hydrocephalus. This work caused Doctor Halsted to say to Doctor Park, "Dandy will never do anything equal to this again. Few men make more than one great contribution to medicine." But Doctor Halsted was mistaken for, in 1918, Doctor Dandy published his epochal paper on ventriculography. Before this technic was developed it had been possible to localize about one-third of all brain tumors. After the method was perfected it was possible to locate virtually every tumor.

Doctor Dandy's intellectual energy was incessant and sustained, as is shown by the continual flow of original contributions which he made to neurosurgery. One need only mention his method for removing acoustic nerve tumors, his successful operations for tic douloureux, glossopharyngeal tic, Meniere's disease, brain abscess, and his treatment of intracranial aneurysms. He was the first to operate for a displaced intervertebral disk, but did not immediately realize the frequency or significance of this lesion.

A careful study of the mind of Walter Dandy revealed three exceptional qualities, and it was the combination of these that accounts for his contributions. First, he had the habit of constantly asking himself searching questions. Second, he had the faculty of going right to the heart of a problem. Third, he had the faculty of seeing and thinking only in absolute terms. Every issue was either black or white, there were no intermediate shades. This all-or-none attitude was characteristic of his relationship to people.

Doctor Dandy was exceptionally daring when operating, but those who assisted him were not impressed by this quality as much as they were by his dexterity. As a technical surgeon he was unrivalled.

Finally, it is right that some comment be made on his ability as a teacher. He fascinated students because his teaching was crystal clear and very positive. His diagnoses on ward rounds were sometimes wrong, but they were never indecisive. His residents received a merciless drill. They were required to follow their postoperative patients hourly, to practice meticulous asepsis, to anticipate every move of their chief when operating. They were slaves, but responsible slaves. The training they received was priceless.

The following tribute had been prepared and was to have been given to Walter Dandy on his sixtieth birthday, but his illness prevented the celebration of the occasion.

"In every field of human endeavor there is occasionally one individual whose achievements set him apart from all his predecessors and above all his contemporaries. Often there is no appreciation of his accomplishments during

his lifetime, and it is left for posterity to acclaim his work. Sometimes, however, the importance of the man's achievements are recognized and some expression of appreciation is given him. This testimonial is such an expression of appreciation, and is given to Dr. Walter E. Dandy in recognition of his accomplishments in the field of neurosurgery. It can be said in all truthfulness that his contributions to this subject are greater than those of any other person. It is fitting, therefore, that the occasion of Doctor Dandy's sixtieth birthday be celebrated by his friends, who give him this portfolio as an enduring emblem of their loyalty to him and of their recognition of his incomparable achievements at the Johns Hopkins Hospital."

WARFIELD M. FIROR, M.D.

## JOHN STAIGE DAVIS

1872-1946

IN THE LATE AFTERNOON of December 23, 1946, while final preparations for family reunions and joyful Christmas festivities were being completed in millions of homes throughout our land, the good people of Baltimore were rudely shocked by the sudden death of one of their most distinguished and best-beloved surgeons, Dr John Staige Davis

My acquaintance with him, which began as a fellow-Virginian, dates back almost to the beginning of our respective careers more than 40 years ago



John Staige Davis

and, through mutual professional interests and activities centering mainly at the Johns Hopkins Hospital and the Union Memorial Hospital, soon ripened into an intimate, congenial and enduring friendship, the memories of which I shall always dearly cherish

Doctor Davis was born in Norfolk, Virginia, January 15, 1872, the son of William B and Mary Jane (Kentie) Howland Davis, and later became the third generation of doctors in the family. His ancestors on both sides from Colonial times were Virginians. At the time of his birth, his father was Assistant Surgeon in the U S Naval Hospital at Portsmouth, Virginia, but later transferred to the U S Army and, as Assistant Surgeon, established a long

record of loyal service to our country Young Staige attended the Episcopal High School of Virginia, 1887-1888, then Saint Paul's School at Garden City, Long Island, which was then a military school, from 1888 until his graduation in 1892 From there he entered Yale University in the Sheffield Scientific School in order to take biologic training under Professor Russell H Chittenden He graduated from Yale in June, 1895, and entered the Johns Hopkins University School of Medicine in the fall of that year, where he obtained his medical degree in 1899 He then served as Resident House Officer at the Johns Hopkins Hospital for one year and as Resident Surgeon and Superintendent at the Union Protestant Infirmary (now the Union Memorial Hospital) under the supervision of Dr J M T Finney for three years Upon completion of his apprenticeship, Doctor Davis was appointed Assistant in Surgery at the Johns Hopkins Hospital Dispensary, and for several years participated in the Surgical Service of the Robert Garrett Children's Hospital He also was Instructor in Surgery at the College of Physicians and Surgeons until that institution was later merged with the University of Maryland

In 1907, he married Kathleen Gordon Bowdoin, whose exceptional charm, conspicuous talents and unfaltering devotion enabled her to create and to maintain that delightfully congenial home atmosphere which contributed so magnificently to his career She now survives him together with one daughter, Mrs Charles E Scarlett, Jr, of Baltimore, and two sons, Major W Bowdoin Davis of the Army Medical Corps, a graduate of Princeton University in 1934, and of the Johns Hopkins University School of Medicine in 1938, who, after serving one year as Surgical Intern at the Union Memorial Hospital, Baltimore, transferred to the Presbyterian Hospital, a unit of the Columbia Medical Center in New York, for several years of intensive apprenticeship in the field of general surgery and as Resident in plastic surgery before being assigned to duty in this specialty at the Valley Forge General Hospital in Pennsylvania He has now been released from the U S Army Medical Corps and, happily, will continue his father's specialty in Baltimore A second son, Howland Staige Davis, established a brilliant record as Lieutenant Commander in the Naval Air Corps during the recent war Five grandchildren also survive

Doctor Davis served as Captain in the Medical Corps of the U S Army during World War I, from June, 1917, to January, 1919 During World War II he was appointed by the Surgeon General of the U S Army as a member of a committee to organize plastic surgery units for the Army Medical Corps He also assisted with his advice and experience at the Walter Reed General Hospital, in Washington, and in other army hospitals during the war years Furthermore he was a member of the Advisory Committee for Medical Preparedness in Maryland, and of the Subcommittee on Plastic and Maxillofacial Surgery of the Division of Medical Sciences of the National Research Council

Early in his professional career he became interested in the mastery and development of plastic surgery, and was the first surgeon to devote himself

exclusively to that field, to the enrichment of which he so brilliantly contributed for 40 years. In 1919, he published a book, "Plastic Surgery Its Principles and Practice," which still is regarded as an authoritative work. In addition, he contributed numerous excellent articles on plastic surgery to various surgical journals. But perhaps his most enduring contribution to the development of his specialty was made through his superb training of a long list of Resident House Officers in the several hospitals with which he was associated. From these inexperienced assistants at the operating table he exacted the same meticulous care of detail that so faultlessly characterized his own work, and, in return, with uncommon clarity, he generously imparted to them from his vast storehouse of knowledge and experience, lessons in plastic surgery that they will never forget and from which many patients will later benefit.

From 1923 to within a brief period prior to his death, Doctor Davis served as Associate Professor of Surgery in the Johns Hopkins University in charge of Plastic Surgery. In addition to this work, he participated actively in the affairs of the Union Memorial Hospital, where for many years he was first a member and later, Chairman of the Executive Committee of the Staff. Throughout most of his active career he served also as Visiting Plastic Surgeon to the Johns Hopkins Hospital, the Union Memorial Hospital, the Children's Hospital School, and the Hospital for the Women of Maryland. He was a member of the American Medical Association, the American Surgical Association, serving as Vice-president in 1937, the Southern Surgical Association, serving as President in 1940, the American Association of Plastic Surgeons, serving as President in 1945, the Interurban Surgical Society, The Baltimore City Medical Society and the Medical and Chirurgical Faculty of Maryland. He was certified by the American Board of Surgery, the American Board of Plastic Surgery and the American College of Surgeons. He was a member of the Military Order of the World War and the Sons of the American Revolution. Just before his death he resigned as Chairman of the American Board of Plastic Surgery, and had just been appointed to the Board of Regents of the American College of Surgeons. He was also a member of the Maryland Club, the Elkridge Club and the Yale Club of New York.

But how imperfectly does this brief recital of some of his achievements in the field of plastic surgery and of the honors so worthily bestowed upon him in recognition of them, portray my friend Staige Davis as I knew him! Creditable, to be sure, is this imposing summary, but it is altogether inadequate. One does not find here the secret of his irresistible personal magnetism which so endeared him to a host of colleagues, friends and grateful recipients of his professional skill. This is to be found rather in the collective attributes of his personality. He was a quiet, gentle person, richly endowed with intellect, sound judgment and an indomitable will, all of which were consecrated to the service of humanity. His sturdy countenance radiated character, honesty, sincerity, kindness, magnanimity, tolerance, sympathy and immeasurable patience. And the motivating force that activated his many virtues was a consuming and sustained desire modestly but efficiently to serve his fellow man, to relieve

suffering, to correct deformities and disfiguring scars and blemishes, to restore function and to abolish the inferiority complexes that so often shackle and torture those unfortunates who require this branch of surgery. All of this he achieved magnificently and, in addition, as teacher, investigator, counselor and consultant, his influence in the development of plastic surgery reached far beyond Baltimore and contributed in no small measure to the rehabilitation of thousands of veterans of two world wars.

He was a member of Saint Paul's Protestant Episcopal Church of Baltimore, and as fine a Christian gentleman as I have ever known.

Approximately one month prior to his death, he was confined to his house for several weeks by order of his physician because of exhaustion from overwork. His prompt improvement was so reassuring, however, that he was permitted to attend the last meeting of the Southern Surgical Association at Hot Springs, Virginia, which both he and Mrs. Davis thoroughly enjoyed. He returned to a slower operative schedule, and on the morning of December 23, 1946, he operated at the Union Memorial Hospital, had office hours, attended to some minor professional duties, and later lunched with a group of his colleagues at the Maryland Club. He was in excellent spirits and appeared to be rapidly regaining his strength. After lunch he rejoined his wife at home and lay down for a period of rest. He quietly and peacefully fell asleep, only to awaken shortly thereafter into a more abundant life which he so richly deserved. His passing is lamented by many, and his loss is indeed a grievous one, not only to his family and intimate friends, but also to Baltimore, the State of Maryland and American surgery.

EDWARD H. RICHARDSON, M.D.

## SAMUEL LABAN LEDBETTER

1886-1946

SAMUEL LABAN LEDBETTER, son of Samuel L. and Nettie Morlow Ledbetter, was born in Birmingham, Alabama, February 26, 1886. He attended the Birmingham public schools, and received the Bachelor of Science degree from the University of Alabama in 1906. He entered the School of Medicine of Johns Hopkins University in the fall of 1906, and received the degree of Doctor of Medicine from that institution in 1910. On graduation, he was



Samuel L. Ledbetter

appointed to membership on the resident staff of the Lakeside Hospital, of Cleveland, where he served for five years, going progressively through the grades of house officer, assistant resident surgeon, and resident surgeon, on the service of the late Dr. George Crile. This association stimulated in him a life-long interest in goiter, and during his active career, he enjoyed a very large clientele of patients suffering from this disease.

When, in World War I the Lakeside Hospital Unit of Western Reserve University was organized, Doctor Ledbetter joined this group and served as resident surgeon, American Ambulance, Neuilly-sur-Seine, in 1915.

After his return from military service, he began the practice of surgery in Birmingham, and was most successful. In addition to holding membership in the County, State and American Medical Associations, he was a fellow of the Southern Surgical Association, of which he was Vice-president in 1937.

of the American College of Surgeons, of which he was a member of the Board of Governors at the time of his death, of the American Association for the Study of Gout, and was a member of the Founders-group of the American Board of Surgery. He was also a member of the Birmingham Surgical Society and the Birmingham Clinical Club. He was surgeon to St. Vincent's Hospital, the Children's Hospital and the Hillman Hospital, and was consulting surgeon to the Woodward Iron Company, the Employees' Hospital of the Tennessee Coal Iron and Railroad Company, Fairfield, and to the American Cast-Iron Pipe Company.

When the Medical College of Alabama was moved from Tuscaloosa to Birmingham in 1945, Doctor Ledbetter was made Clinical Professor of Surgery but ill health prevented him from taking active part in the work of the College.

In spite of the demands of his large surgical practice, Doctor Ledbetter was much interested in sports and in the social activities of the city. He spent many leisure hours in hunting and fishing, was a member of the Mountain Brook Country Club, and was keenly interested in football.

In 1918, he married Frances Hoke Robinson, of Easley, South Carolina. She and a daughter, Miss W. W. McPhillips, and two grandchildren survive him.

Doctor Ledbetter was an active member of the Episcopal Church.

His illness was prolonged and, in the latter months, painful. For years he carried on bravely and actively, knowing full-well the fate that awaited him. Several operations were undertaken for relief of complications that arose from time-to-time. Finally he had to give up the struggle, and died on March 10, 1946.

JAMES M. MASON, M.D.



## JOHN CHADWICK OLIVER

May 7, 1862–March 14, 1946

THE OLIVERS came early to the western country, in fact Dr David Oliver, grandfather of John C , was the first white child born among the pioneers of the Marietta Colony on the Muskegon in the year 1792 He was the son of New England frontiersmen who followed General Israel Putnam to the Ohio country before the turn of the nineteenth century Dr David Oliver grew up and came to Cincinnati where he practiced his profession in the West End many years ago It is not stated whether he knew well, or had much connection



John Chadwick Oliver

with Dr Daniel Drake but the two were in Cincinnati at about the same time

Doctor Drake, known as the father of western medicine, founded the Ohio Medical College in Cincinnati in 1819, and, later on, just to show that he could, he founded the Miami Medical College as a branch of the Miami University at Oxford, Ohio in 1852 It was at this latter college that Dr John Oliver attended and, at the age of 23, namely, 1885, he graduated with honors

Dr Cornelius George Comegys, a contemporary of Daniel Drake, took Doctor Oliver into his office as his assistant Doctor Oliver immediately began to serve his Alma Mater as demonstrator in anatomy and later as professor of

anatomy Under Doctor Comegys' tutorage Doctor Oliver progressed rapidly in his chosen profession and upon his friend's demise, in 1896, he became associated in the practice of surgery with the greatly loved and esteemed Dr N P Dandridge, then Dean of the Miami Medical College

Later, Doctor Oliver himself became Dean of that honored institution and, as such, initiated the movement to unite the Miami Medical College with the Ohio Medical College After a long bitter struggle this was done to form first, the Ohio-Miami Medical College of the University of Cincinnati and later the name was shortened to the College of Medicine of the University of Cincinnati

After the death of Dr Christian R Holmes in 1920 Doctor Oliver became Dean of the College of Medicine of the University of Cincinnati After serving in that capacity for several years he resigned

Doctor Oliver was a cultured gentleman of strict integrity and a great surgeon As a teacher and a colleague he set an example of faithful observance in medical ethics As a writer he was clear and concise In the writings in the local journals and the annals of the American Surgical Association and the Southern Surgical Association many contributions may be found

In October, 1888, he married Carrie Frances Wright who bore him three children Dr Wade Wright Oliver, the eldest, is now the Professor of Bacteriology at the Long Island Medical College Dr Symmes Francis Oliver, a surgeon in Cincinnati, is at present connected with the Veterans' Bureau, and a daughter, Sarah Elizabeth Kerper, lives in Washington, D C

In 1902 Doctor Oliver was elected to the Southern Surgical Association and came regularly for a good number of years However, age and ill health have kept him away for the last few years, but those of us in and about Cincinnati knew him well and will sadly miss him

RALPH G CAROTHERS, M D

### NEW EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

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## BOOK REVIEW

**MEN WITHOUT GUNS** Text by DeWitt Mackenzie Descriptive captions by Major Clarence Worden Foreword by Major General Norman T. Kirk Illustrated with 137 colored plates Blakiston Co., Philadelphia, 1945

"MEN WITHOUT GUNS" is a combination of narrative and illustrations giving that part of the history of World War II that deals with the care of the wounded from the forward areas and battle fronts of the various theaters back to the large hospital centers within the United States. The various theaters, beginning with the Southwest Pacific, are treated separately, both as to text and sketches. A foreword by the Surgeon-General, Norman T. Kirk, M. C., U. S. A., emphasizes the heroism and skill of the men and women of the Army Medical Corps. He properly lists three of the war's outstanding innovations in establishing an excellent record for the care of the wounded—surgery, the sulfa drugs, and penicillin. Qualifying this, he says "Surgery is Number One, it isn't the sulfa drugs that save lives, it's surgery, drugs supplement surgery." The brief summary of General Kirk's accomplishments in meeting the tremendous task of caring for the wounded is well done.

In considering the function of the Army Medical Corps, one might judge from this book that the difficulties were for the most part the result of combat conditions, the weather and terrain in particular. Many of the medical officers of the Army may well question this from their experience because the successful accomplishment of the day's work in the Medical Corps was often in spite of existing cumbersome Army regulations so religiously adhered to by old regular Army officers. However, now that the war has been successfully completed it may be just as well to indulge in a little euphoria from the standpoint of making the review of it as pleasant as possible. Nevertheless, in fairness to those of the medical profession who may participate in the next war, greater emphasis should be placed upon the long periods of waiting and the possibility of improper assignments rather than the physical hardships of the tropical mud and mould or the Normandy cold and blitz bombs.

The medical corpsman is the hero of this book and rightfully so because of all the tasks that any member of the Medical Department of the Army is called upon to do no other requires as much bravery, singleness of purpose, and clearness of mind under fire. These men, common to every medical unit near a front, are pictured in action.

The twelve artists who have contributed to this volume have by great attention to detail plus the knowledge that comes from being on the spot during action given an accurate picture of various aspects of caring for the wounded of this war. They are earthy, they carry the background of the situation, they present much in one sketch, sometimes it may have been added onto from their memory but, regardless, it reveals what was then taking place. In these illustrations there is a virile integrity that pervades the entire book which is admirable. There has been no magnification of the horrors nor has there been covering up of the unpleasant. A short biography of each artist, including his assignment and contributions, adds to the reader's personal interest in each group of paintings and sketches. That these artists escaped without major mishap in their assignments is remarkable. Over two-thirds of the book consists of paintings and sketches without duplication.

This book will appeal in particular to the doctors, nurses, and corpsmen of the Army of World War II. Those who were overseas will find their greatest interest in those paintings and sketches from the theater in which they served, be it Southwest Pacific, Burma-India, or European. It is not likely to have more than passing attention from those who were not in some way directly concerned with the care of the wounded.

FRANK GLENN, M.D.

THE MANAGEMENT OF CARCINOMA IN THE  
SEVERAL PARTS OF THE COLON\*

WILLIAM F. MACFEE, M.D.

NEW YORK, N Y

THOUGH NOT THE FIRST to practice delayed extraperitoneal resection in the surgical treatment of carcinoma of the colon, Mikulicz,<sup>1</sup> in 1903, was the first to report a series of cases treated in this manner. His publication of the results in 16 cases in which the carcinoma was first brought out of the abdominal cavity and later excised had a profound effect upon the surgical treatment of this disease. The principle of extraperitoneal resection became established almost immediately and still attracts many followers.

Acceptance of the exteriorization method, though widespread, was not universal. It has disadvantages in certain types of cases, particularly in obese patients with short mesentery, and interest in finding a safe method of performing primary resection and anastomosis was not lost.

The search took two general directions. First, there was the quest for an effective aseptic method of performing resection and anastomosis, and, second, efforts were directed toward getting the bowel into better condition before resection and suture were attempted. The endeavor to find a way to maintain asepsis led to the development of ingenious clamps and other devices intended to accomplish that purpose. Wangensteen,<sup>2</sup> who himself designed a clamp for anastomosis, states that Parlavecchio, an Italian surgeon, used a similar clamp as early as 1898 to 1900. The names of Parker and Kerr,<sup>3</sup> Schoemaker,<sup>4</sup> Fraser and Dott,<sup>5</sup> Scarff,<sup>6</sup> Rankin,<sup>7</sup> and many others, are associated with methods of aseptic, or closed, anastomosis.

The importance of having nondistended bowel of normal texture before resection and anastomosis are attempted was brought home to the earlier surgeons through grievous experience. It was gradually recognized that a high operative mortality prevailed when obstruction was present and a relatively low mortality, even with open anastomosis, when obstruction was

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\* Read before the New York Surgical Society, December 11, 1946

absent. The advantages of having normal bowel to deal with became clear, and when medical means of evacuation were ineffectual it was natural that surgical drainage should be considered. According to Rankin,<sup>8</sup> the idea of external drainage of the distended bowel proximal to an obstruction was entertained as early as 1710 by Littre, who proposed colostomy for relief of obstruction due to malformation of the rectum, but it remained for Pillore, of Rouen, 66 years later, to actually perform a right inguinal colostomy for obstruction of the rectum due to tumor.

It is not clear who was the first to make a practice of draining the colon proximal to an obstructing growth in preparation for its removal. It may well be that the first colostomies producing this effect were more or less accidental. Hartwell,<sup>9</sup> for example, describes opening the abdomen for intestinal obstruction and finding a band over the distended cecum which had produced a slough. There was gross leakage, and to meet the situation he made a right intermuscular incision and sutured the margins of the hole in the cecum to the incised peritoneum and to the skin. Without previous design he, thus, established a cecostomy. The patient improved to such an extent that the obstructing tumor, a carcinoma of the splenic flexure, was later removed and the patient survived. Whatever the origin of the operations for proximal drainage of the colon, their usefulness in the presence of obstruction and other complications is now generally recognized. Mayo,<sup>10</sup> Bevan,<sup>11</sup> Cline,<sup>12</sup> Stiles,<sup>13</sup> Schoemaker,<sup>14</sup> Cheever,<sup>15</sup> Whipple,<sup>16</sup> Rankin,<sup>17</sup> Wilkie,<sup>18</sup> and Allen,<sup>19</sup> have had a noteworthy influence in developing an appreciation of these procedures.

The lowering of mortality has been accomplished not only by improved surgical management but also by a number of other factors. The introduction of the sulfonamide drugs, particularly the intestinal antiseptics succinylsulfathiazole (sulfasuxidine) and phthalylsulfathiazole (sulfathalidine) the efficacy of which has been demonstrated by Poth,<sup>20</sup> the more effective intestinal deflation by use of the Miller-Abbott tube, greater alertness in early diagnosis, and the increased competence of a greater number of surgeons, all have contributed to the safety of the operation. In addition to these advantages, there is a better understanding of the pathologic physiology associated with surgical operations, greater appreciation of the importance of fluid and protein balance, of vitamins, blood transfusion, and the numerous collective measures which have contributed to the improvement of surgery in general.

As the safety of primary resection and anastomosis has increased, and fewer patients arrive with obstruction, there has been a growing tendency toward the performance of a one-stage instead of a two- or three-stage operation. Right colectomy for lesions without obstruction has long been performed as a one-stage procedure, but in the presence of obstruction or other complications resection has been preceded by ileocolostomy. Whipple,<sup>21, 22</sup> has reported strikingly favorable results from the use of the Miller-Abbott tube as a preoperative means of deflation, and finds that obstructive lesions of the right colon which previously would have required preliminary ileocolostomy may now be resected in one operation.

## CARCINOMA OF THE COLON

In planning the resection of an uncomplicated carcinoma, Campbell,<sup>23</sup> Stone and McLanahan,<sup>24</sup> Wangensteen,<sup>2, 25</sup> Waugh and Custer,<sup>26</sup> Meyer, Sheridan, and Kozoll,<sup>27</sup> and Zininger and Hoxworth<sup>28</sup> no longer differentiate between the right and left portions of the colon, and may undertake a one-stage operation irrespective of the location of the tumor. They believe primary one-stage resection and anastomosis is safe in the left colon as well as in the right, provided there is minimal or no obstruction or other serious impediment.

Considerable differences of opinion are found among the large clinics of this country concerning the merits of various operative procedures, particularly with respect to the Mikulicz-type of operation. Undoubtedly, these divergences of view have created uncertainty in the mind of the general surgeon who operates upon the occasional case. His experience with the disease has not been sufficient to permit him to have definite ideas based upon personal observations, and a review of the literature does not enable him to see clearly the course he should pursue.

On the one hand, he has the opinion of Lahey,<sup>29, 30, 31</sup> whose vast experience has confirmed him in the belief that the modified Mikulicz procedure is the safest operation for carcinoma of the large bowel, including the right colon. With respect to the right colon, however, there appears to be some deviation<sup>32</sup> from this rule. Almost diametrically opposed is Wangensteen<sup>2</sup> whose practice is to resect all unobstructed lesions of the colon in one stage, establishing intestinal continuity by oblique aseptic end-to-end anastomosis without antecedent or complementary colostomy or decompressive vents. Among those following a middle course are Rankin,<sup>33</sup> Allen,<sup>19</sup> White and Amendola,<sup>34</sup> and Coller and Vaughan<sup>35</sup> who may do either an obstructive resection or resection with immediate end-to-end anastomosis, but when the latter operation is elected ordinarily establish proximal drainage either as a preliminary measure or at the time of resection, except in unobstructed lesions of the right colon.

The results at the Lahey Clinic, where the modified Mikulicz procedure has been followed almost exclusively in the treatment of hundreds of cases, the results have been excellent. Whether they would have been better with resec-

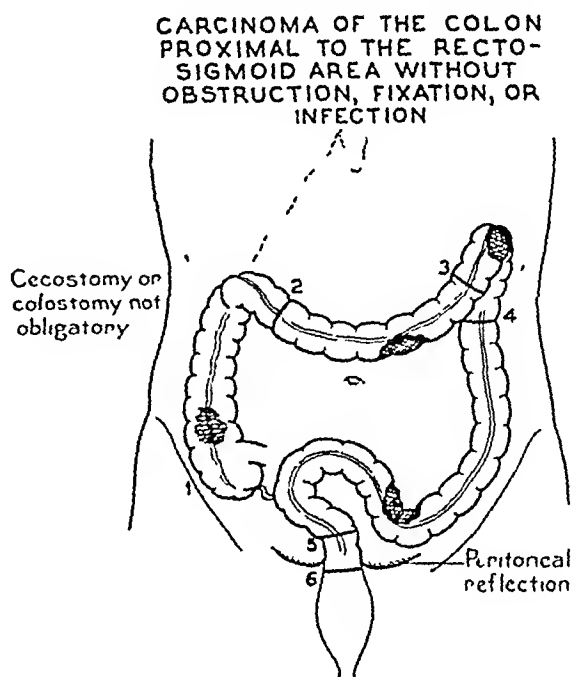


FIG 1—Colon divided into surgical segments  
1-2 Cecum, ascending colon, and hepatic flexure  
2-3 Transverse colon  
3-4 Splenic flexure  
4-5 Descending colon and sigmoid  
5-6 Rectosigmoid

The diagrammatic representation of a tumor is shown in each segment except the rectosigmoid.

tion and anastomosis we cannot know. As between the principles of exteriorization, and resection with aseptic end-to-end anastomosis, there can be little question but that the present trend is in favor of the latter procedure, with or without proximal drainage.

In hospitals where both types of operations are done in something like equal numbers the results generally favor closed resection and anastomosis. In a series of cases reported from St. Luke's and the New York Hospitals<sup>36</sup> the mortality was appreciably higher with the exteriorization procedures. In a subsequent study of cases from the Pennsylvania and Bryn Mawr Hospitals Gibbon and Hodge<sup>37</sup> found the mortality from exteriorization procedures more than twice that following closed resection with aseptic anastomosis, and in a compilation of statistics which included other clinics,<sup>36, 38, 24</sup> as well as their own, the mortality from exteriorization operations was 27 per cent, and for resection with aseptic anastomosis 14 per cent. In 1940, Patterson and Webb,<sup>39</sup> basing their study on cases treated at the Roosevelt Hospital, reported favorably on the Mikulicz procedure, but four years later, after having given aseptic resection and anastomosis a trial, White and Amendola,<sup>34</sup> in a review of cases from the same institution, found that the mortality from the Mikulicz operation was twice that resulting from resection with aseptic anastomosis. With these facts in mind, the present discussion of treatment will be concerned primarily with the latter method.

To attempt the formulation of rules to meet all the conditions which may complicate carcinoma of the colon or to prescribe operative procedures for all to follow would be presumptuous and futile. One cannot, however, review the experience of the many surgeons who have had a special interest in this disease and correlate it with his own without arriving at certain conclusions as to how carcinoma of the colon, as ordinarily encountered, should be treated.

If one elects closed resection with aseptic anastomosis, there are certain basic principles which must be observed. These were very well presented by Reichel,<sup>40</sup> in 1911:

- 1 The general condition of the patient must be such that a somewhat lengthy operation is permitted.
- 2 The intestine proximal to the tumor must not harbor any considerable accumulation of fecal material.
- 3 The intestine must be viable and free of circulatory disturbance.
- 4 It must be possible to suture the ends of intestine together without tension.

Reichel, furthermore, admonished care in placing the sutures so that the approximation should be accurate. He believed that poor results were due to emphasis upon speed of operation rather than upon exactitude. Little fault is to be found with Reichel's criteria, and if any one condition is to be stressed above the others it is that the intestine must be viable and free of circulatory disturbance. Such favorable conditions cannot exist in the presence of obstruction.

It may be stated as a corollary to Reichel's rules, that if the bowel is not

in a suitable state for primary resection and anastomosis, the operation should not be attempted until the adverse conditions have been corrected. Any restriction upon immediate resection, such as obstruction, local infection, or fixation, must be corrected before the definitive operation is attempted. In the occasional case it is impossible to attain wholly favorable conditions for operation and known risks must be accepted. However, the surgeon in his desire to hasten the patient's recovery must not be tempted to take risks which might be avoided by a less hasty plan.

For the purpose of discussing operative procedures, the colon often is divided simply into right and left halves. The problems of surgical management of carcinoma in certain parts of the two main segments, however, require more specific treatment and for convenience in discussion a more detailed segmentation is offered (Fig 1). Consideration will be confined largely to surgical management and surgical principles rather than to technical details, such as methods and materials employed. These have been considered in a previous publication,<sup>36</sup> and are described in a number of recent contributions<sup>23, 2, 28, 41</sup>

#### CARCINOMA WITHOUT OBSTRUCTION, FIXATION, OR INFECTION

It is becoming increasingly evident that in the absence of obstruction, fixation, or infection, a carcinoma in almost any part of the colon may be resected and continuity immediately restored without undue risk. Appreciable obstruction, fixation, or infection are contraindications. In dealing with the right colon, Whipple's<sup>22</sup> more recent experience has led him to believe that with suitable preparation of the bowel and care in performance the open suture technic is as safe as the so-called aseptic methods. Meyer, Sheridan, and Kozoll<sup>27</sup> have arrived at similar conclusions with respect to the left colon. This does not agree with the findings of Stone and McLanahan.<sup>24</sup> It would appear logical that the closed technic involves less contamination and is the better procedure.

In conceding the general applicability of primary resection and anastomosis to the uncomplicated carcinoma of the colon, reservations should be made with respect to the splenic flexure and the rectosigmoid segment. These will be discussed under the appropriate headings.

#### CARCINOMA WITH OBSTRUCTION, FIXATION, OR INFECTION

The presence of appreciable obstruction, fixation, or infection in association with a colonic carcinoma precludes the safety of immediate resection and anastomosis. The harmful effects of obstruction on the blood supply, viability, and tenacity of the proximal bowel wall are well-known and are more important than the bowel content.

The dangers of fixation reside in the fact that it renders mobilization difficult, and adjacent structures may be damaged by attempts to free the tumor. Furthermore, fixation may be associated with infection, often with abscess.



formation, and efforts to detach the tumor from its surroundings may lead to gross contamination through accidental opening of the bowel, or by breaking into an abscess. The importance of draining the proximal obstructed colon for a period of several days before resection is attempted, and the risks of failure to drain cannot be questioned.

With the general principles of resection in mind we may proceed to a more detailed discussion of treatment according to the part of colon involved.

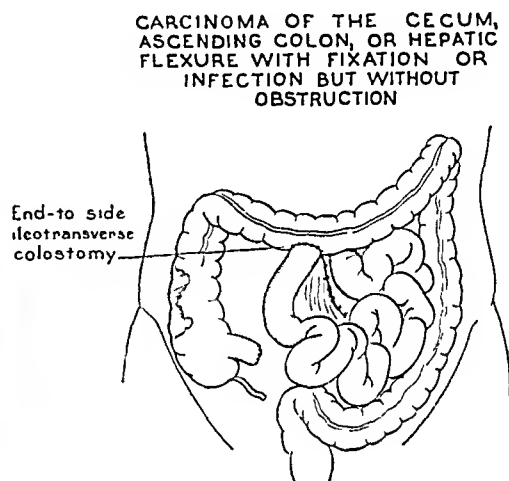
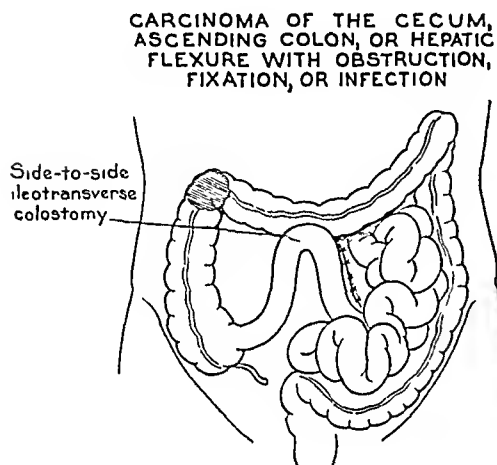


FIG 2—Obstructing carcinoma of the right colon (hepatic flexure) with side-to-side ileotransverse colostomy performed. Note closure of space between mesenteries of terminal ileum and transverse colon.

FIG 3—Carcinoma of right colon with fixation or infection, but without obstruction. End-to-side ileotransverse colostomy has been done, and closed end of distal segment of ileum returned to usual position.

## I CECUM, ASCENDING COLON, AND HEPATIC FLEXURE

This portion of the colon, constituting almost its entire right half, may be discussed as a unit, operative treatment for carcinoma in any part of it is essentially the same. The treatment consists of resection of the entire segment with restoration of continuity by ileotransverse colostomy. In the absence of obstruction, fixation, or gross infection, the operation is ordinarily done in one stage. If obstruction is present a preliminary side-to-side ileotransverse colostomy is done (Fig 2), with resection following in approximately two weeks. If fixation or infection is present without obstruction, an end-to-side ileotransverse colostomy may be done and the closed distal end of the ileum returned to the abdominal cavity (Fig 3). After the preliminary ileotransverse colostomy, inflammation subsides, at the second operation the mass often is found surprisingly mobile and may be resected with ease.

With either procedure, it is important to close the opening between the mesentery of the proximal segment of ileum and that of the transverse colon. Allen<sup>19</sup> mentions a fatal case of obstruction of the small bowel from herniation

through the trap left by the preliminary ileotransverse colostomy. After ileocolostomy has been completed, there should be no resort to external drainage of any kind. It accomplishes nothing and carries with it all the dangers and disagreeable features associated with external small intestinal fistulae.

In doing a closed ileocolostomy, one must be sure that the triangular piece, or pieces, of bowel wall grasped by the clamps include mucosa. This can be determined by inspecting the portions of wall removed. To be sure of patency after anastomosis the finger is used to invaginate bowel wall through the stoma.

One may ask why it is necessary to do a complete extirpation of the right colon, even for a small tumor of the cecum or ascending colon. The answer lies mostly in the fact that the ileocolic group of lymph nodes, as Jameson and Dodson<sup>42</sup> found, extends as high as the duodenum. The distribution of the blood supply is also a consideration. Steward and Rankin,<sup>43</sup> and Singleton<sup>44</sup> have called attention to rather frequent anomalies of the blood vessels of this and other parts of the colon. Resection of the right colon is sometimes regarded relatively safe as compared with the more distal segments. Allen,<sup>19</sup> however, reminds us that in most clinics operative mortality remains greater in this segment than elsewhere.

CARCINOMA OF THE TRANSVERSE COLON, WITH OBSTRUCTION, FIXATION, OR INFECTION

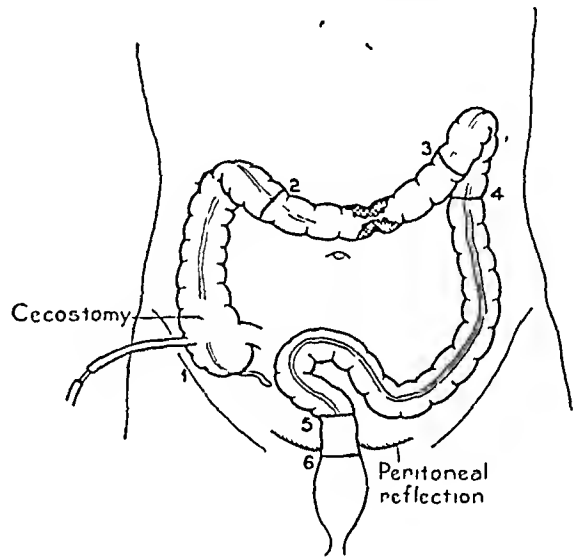


FIG 4—Carcinoma of transverse colon with obstruction, fixation or infection. Drainage of proximal colon by cecostomy.

## 2 TRANSVERSE COLON

In this segment, due to its large caliber and fluid content, obstruction is the exception. Furthermore, the transverse colon is relatively superficial and tumors situated in it may be felt before they reach large size. Tumors of the transverse colon ordinarily are well-suited to primary resection and anastomosis without proximal drainage. Mayo and Simpson,<sup>45</sup> reporting a series of cases, found that the mortality for exteriorization procedures was 20 per cent, whereas the mortality following resection with primary anastomosis was 11.1 per cent. The middle colic artery comes in for special consideration because of the dependence of almost the entire transverse colon upon it and the frequent necessity of resecting a portion of it with the tumor. The viability of the ends of colon to be sutured together must be assured before the anastomosis is made. In some cases it is necessary to mobilize the splenic or hepatic flexure in order to bring viable ends together.

In the occasional case with obstructions, proximal deflation can be satis-

factorily accomplished by cecostomy (Fig 4) If distention is extreme, and the cecal wall is greatly thinned, it is better, as Rankin<sup>17</sup> suggests, to seal off the anterior cecal wall and deliberately puncture it with a small needle After the gas has escaped the cecostomy can be performed with less danger of accidental rupture The bowel should be irrigated daily to insure evacuation of the

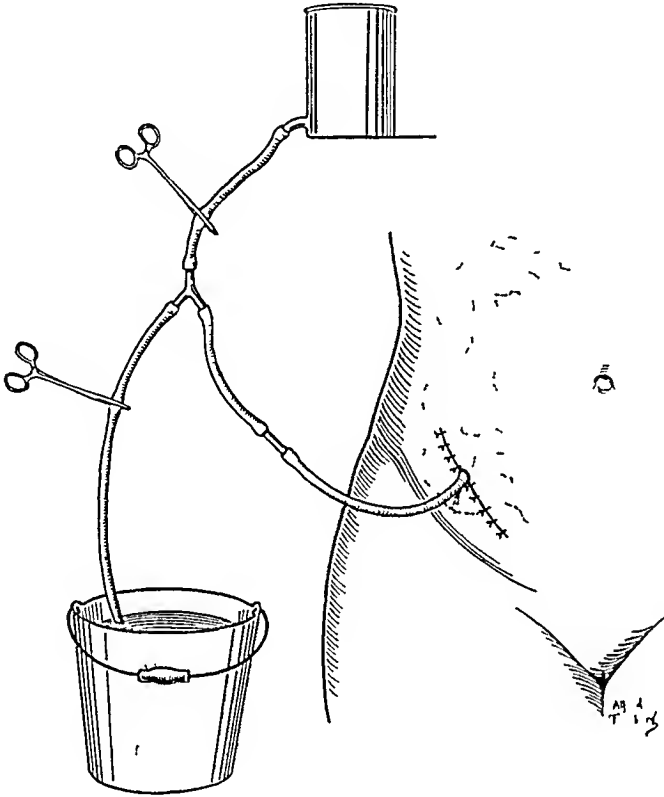


FIG 5—Simple apparatus for irrigating colon through cecostomy prior to resection The flow of water from irrigating can is controlled by means of the two hemostats The cecostomy tube is a mushroom (Pezzar) catheter, the tip of which has been cut off The fecal return is received by the pail below

accumulated feces and to keep it deflated A convenient apparatus for this purpose is shown in Figure 5 As a rule, ten to 14 days after cecostomy, resection can be carried out with safety Irrigations should be suspended until the anastomosis is secure and then resumed with care As soon as bowel movements by rectum have started, the cecostomy tube may be withdrawn and the wound given opportunity to heal If spontaneous healing fails or is long delayed, the opening may be closed surgically

### 3 SPLENIC FLEXURE

The splenic flexure comprises the splenic angle with approximately 10 cm of colon on either side Carcinoma arising in this segment requires special consideration for several reasons

## CARCINOMA OF THE COLON

1 The symptoms, due mainly to beginning obstruction, are obscure, and are often referred to parts of the abdomen remote from the site of the tumor. The treatment for a long period of time may be based on an erroneous diagnosis.

2 Tumors of the splenic flexure ordinarily are high under the costal margin near the posterior abdominal wall and cannot be palpated until they reach large dimensions.

3 The proximal segment of the splenic flexure lies anterior to the distal segment and a carcinoma situated in either may not be revealed by the usual

CARCINOMA OF THE DESCENDING OR SIGMOID COLON WITH OBSTRUCTION, FIXATION, OR INFECTION

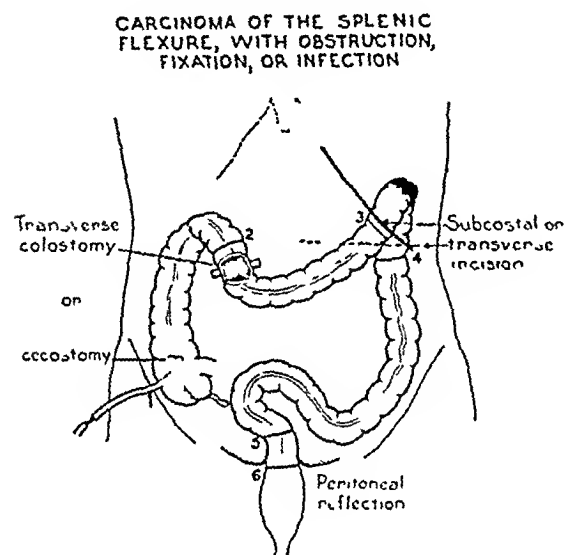


FIG 6—Carcinoma of splenic flexure with obstruction. Proximal deflation and drainage are effected by cecostomy or transverse colostomy. Fixation or infection require the same treatment. Possible approach through anterior subcostal or transverse incision is indicated.

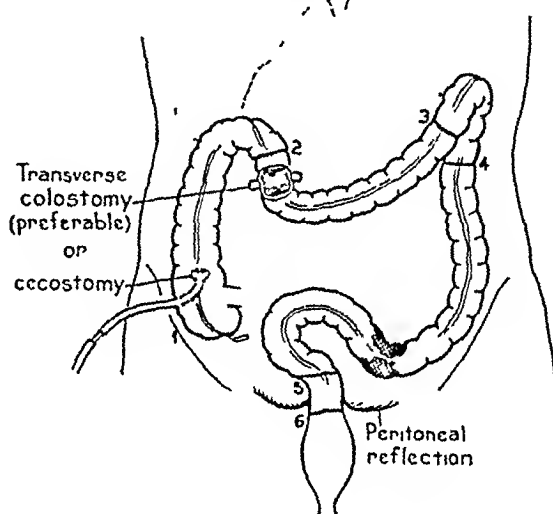


FIG 7—Carcinoma of descending or sigmoid colon with obstruction, fixation, or infection. Proximal drainage by cecostomy or transverse colostomy, preferably the latter, is required. Resection should be delayed 10 to 14 days.

anteroposterior roentgenogram. If examinations are not made in the oblique view the tumor is likely to be missed.

4 Tumors in the splenic flexure are frequently of the annular type and complete obstruction is often the symptom that leads to recognition.

5 Because of the delay in diagnosis, perforation with abscess formation is common in this region.

6 Fixation of the tumor is a frequent complication.

7 Surgical access is difficult, particularly in obese patients.

All of these possibilities forecast the frequency of complications in carcinoma of the splenic flexure and warrant the setting apart of tumors in this region for particular attention. Preliminary cecostomy, or transverse colostomy will prove an aid often enough to justify routine use. Proximal drainage is seldom a disadvantage, and may be extremely helpful.

The surgical approach to the splenic flexure usually is more difficult than that to other segments and an anterior subcostal, or transverse incision is advantageous (Fig 6) An incision below and parallel to the posterior rib margin, described by Hoag,<sup>46</sup> appears to have merit Exaggerated fear in regard to healing of the transverse incision and its modifications need not be entertained

#### 4 DESCENDING COLON AND SIGMOID

Enough experience has accumulated to prove that uncomplicated tumors in this segment may be resected without serious risk after a thorough preparation of the bowel by conservative means Annular growths producing par-

CARCINOMA OF THE RECTOSIGMOID  
AREA WITH OR WITHOUT  
OBSTRUCTION, FIXATION, OR  
INFECTION

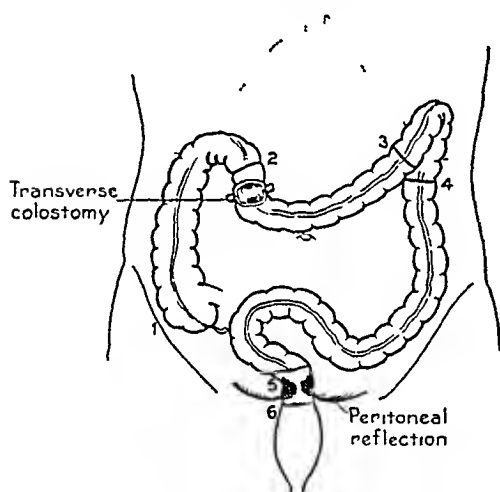


FIG 8—Carcinoma at the rectosigmoid with or without obstruction Complete diversion of feces by transverse colostomy 10 to 14 days prior to resection is required If the tumor is fixed, or gross infection is present, the success of anastomosis to the lower segment is doubtful

tial or complete obstruction, however, are common in the long segment of colon When there is a history of intermittent or persistent obstructive symptoms or evidence of fixation or infection, it is safer to do a cecostomy or transverse colostomy (Fig 7) and delay resection until the bowel has had a sufficient period of deflation to regain its normal properties Ordinarily this is a matter of 10 to 14 days, depending upon the degree of obstruction or the severity of other complicating factors

The differentiation between diverticulitis and carcinoma is sometimes a problem The two conditions simulate each other very closely There are few symptoms of one which cannot be attributed to the other The demonstration of diverticula in the roentgenograms does not rule out

cancer The diagnosis can be established in most instances by repeated fluoroscopic observations with the aid of the barium enema If drainage of the proximal bowel is carried out in the belief that an obstruction is caused by carcinoma when in fact it is due to diverticulitis, roentgenograms taken several days later may show that the obstruction has largely disappeared When diverticula are known to be present, it is well to repeat the roentgenologic examination before resection of a lesion presumed to be carcinoma is undertaken

The descending colon often requires considerable mobilization before satisfactory anastomosis can be established but it must be freed even more if an exteriorization procedure is done The sigmoid, because of its length and mobility, is perhaps the most adaptable part of the colon for the Mikulicz-type of operation, but for the same reasons it also lends itself well to resection and immediate anastomosis

### 5. RECTOSIGMOID

This segment of colon (Fig 8) has been variously defined, but for practical purposes a tumor may be said to be in the rectosigmoid when its excision requires transection of the bowel below the level of the reflection of the pelvic peritoneum. After the resection of such a tumor, the success of an end-to-end suture is imperiled by certain characteristics of the lower segment which limit its adaptability for secure union with the upper segment.

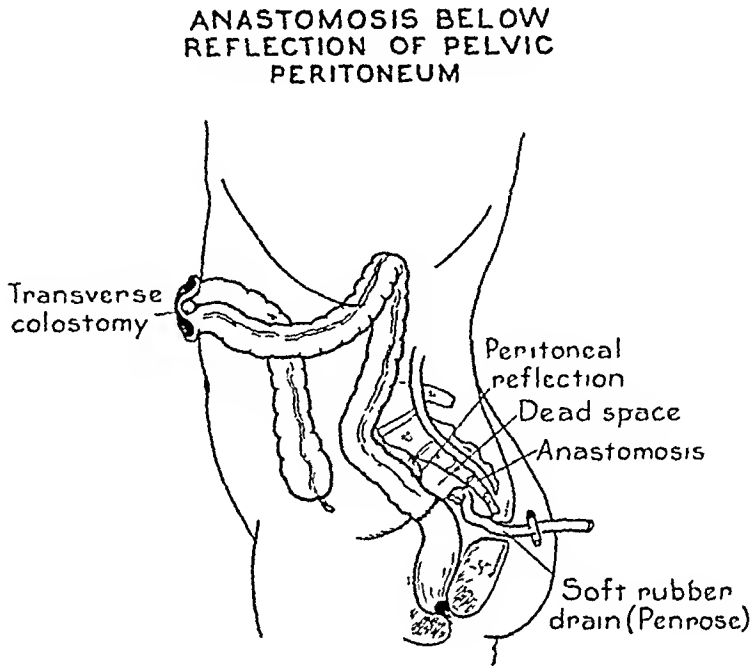


FIG 9—Drainage of space about anastomosis situated below pelvic peritoneal floor is accomplished by resecting the coccyx and inserting a soft rubber drain of the Penrose-type through its bed

- 1 The lower segment lacks the visceral peritoneal investment which contributes so much to dependable apposition and prompt healing
- 2 The perirectal tissues lying below the pelvic peritoneal floor are highly susceptible to infection
- 3 Surgical access to this region is difficult

In spite of these disadvantages there has been no lack of effort on the part of surgeons to restore continuity of the bowel and preserve the function of the sphincters. Kraske's<sup>47</sup> operation, described in 1885, was designed primarily for high carcinomas of the rectum, and when possible restored continuity by suture through a sacrococcygeal approach. Hochenegg<sup>48</sup> brought the upper segment of resected bowel down through the rectal sphincters and sutured it to the anal margin. Balfour<sup>49</sup> introduced through the rectum a large tube to which the upper segment was attached and partially telescoped into the lower. Crile<sup>12</sup> did a low end-to-end anastomosis through an abdominal approach in much the same manner the operation is now performed by Dixon,<sup>50, 51</sup> and Wangenstein.<sup>2, 25</sup> Crile preceded the operation by a complete diversion of the

fecal stream through a transverse colostomy. In addition to a transabdominal operation for the resection of carcinomas eight centimeters, or more, from the anal outlet, Mahorner<sup>52</sup> has described a technic for combined abdomino-ischial resection, applicable to low rectal growths, with preservation of the sphincters.

Resection of carcinoma of the rectosigmoid with end-to-end suture through an abdominal approach is a practicable operation in the average case. As the level of the tumor descends, however, the risks of the operation rise rapidly. Rather frequent infection and leakage at the site of anastomosis have been recorded by Wangensteen,<sup>25</sup> and by Waugh and Custer.<sup>26</sup> Wangensteen, who performs the operation without preliminary drainage or diversion of feces in the proximal colon, reported primary healing in only a minority of anastomoses following resection of tumors less than 10 cm from the anus. Waugh and Custer mentioned cases in which there was drainage of an abscess into the rectum.

The risks of leakage and infection are materially reduced if the line of anastomosis falls within the peritoneal cavity, or if the pelvic floor can be reestablished below the anastomosis, as recommended by Allen.<sup>19</sup> Intraperitoneal resistance to infection is greater than that of the extraperitoneal tissues and healing is promoted by the adherence of peritoneum at the suture line. If the anastomosis necessarily lies below the peritoneal floor, drainage of the surrounding space is a required measure. This can be done suprapubically, as practiced by Dixon<sup>50, 51</sup> or through an opening established immediately anterior to the tip of the coccyx, as advocated by Wangensteen.<sup>25</sup> More effective drainage, however, is secured by removing the coccyx and establishing a vent through its bed (Fig 9). The drain should be of thin, soft rubber, such as the Penrose-type. A thick or hard tube may impinge on the bowel and produce necrosis. The judicious use of the antibiotic drugs affords considerable security against fulminating infection in this region. One of the greatest single measures of safety in resection and suture at the rectosigmoid level is a transverse colostomy performed several days in advance and completely diverting the feces.

In their conclusions, Stone and McLanahan<sup>24</sup> regard immediate resection, immediate anastomosis, and utilization of aseptic technic as the ideal type of operation for carcinoma of the colon. There can be no disagreement with this definition of the ideal, which finds practical application in the uncomplicated case. The drawback resides in the fact that it is often impossible to know in advance just what complications, if any, exist, and what measures may be necessary to cope with them. There may be, for example, an unsuspected inflammatory process about the tumor, multiple adhesions of other viscera to it, or a walled-off perforation. If the bowel proximal to the lesion has first had a period of partial or complete rest through cecostomy or colostomy, it should be in the best possible condition for whatever operative procedure is necessary.

When primary resection is intended and an unforeseen complication is encountered, there is always the inclination to proceed with the definitive

operation as planned, bearing in mind, but at the same time disregarding, the fact that conditions for the operation are not ideal. The result may be chastening to the surgeon, and irreparably bad for the patient. If exploration reveals that immediate resection and anastomosis are definitely not practicable, the decision to do a cecostomy or transverse colostomy, and wait, is not difficult. It is the middle ground case that offers the greatest temptation and, therefore, the greatest danger.

### CONCLUSIONS

1 Uncomplicated carcinoma of the cecum, ascending colon, and hepatic flexure may be resected and ileotransverse colostomy performed at a single operation. In the presence of obstruction, fixation, or infection, ileotransverse colostomy should be done first with resection following later.

2 Carcinoma of the transverse colon ordinarily may be resected and anastomosis established as a one-stage operation. Obstruction, extensive fixation, or infection calls for a preliminary cecostomy.

3 Carcinoma of the splenic flexure is often recognized late, complications are frequent, and surgical approach may be difficult. Preliminary cecostomy or transverse colostomy should be the rule, with primary one-stage resection reserved for the exceptional case. Transverse, or subcostal incision provides a good exposure.

4 In the descending and sigmoid colon, primary resection and immediate anastomosis are permissible provided there are no complications. Obstruction, fixation or gross infection requires proximal drainage by cecostomy or transverse colostomy, preferably the latter. Diverticulosis may confuse the diagnosis and treatment.

5 At the rectosigmoid level, preliminary transverse colostomy with complete diversion of feces is a prerequisite to resection with immediate anastomosis. Faulty healing of the suture line frequently results in leakage, infection, and fistulae. The presence of feces in such a field is a serious disadvantage.

6 The space about an anastomosis established below the level of the pelvic peritoneal floor should be freely drained through the coccygeal bed.

7 Primary one-stage resection and anastomosis may succeed in any part of the colon proper, but it should not be performed for tumors in the rectosigmoid and its use elsewhere should be limited to uncomplicated lesions.

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# CARCINOMA OF THE THYROID

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ALTHOUGH most thyroid cancer occurs in nodular goiters, the incidence of malignant tumors in nodular goiters has been regarded by many physicians as too low to be accepted as a valid indication for their routine removal. However, as the operative risk has declined, it has become probable that life can be saved by taking a more radical attitude toward nodular goiters. This view was recently emphasized by Hinton and Lord<sup>10</sup> who found the incidence of carcinoma to be 7.6 per cent in clinically benign nodular goiters as compared to an incidence of 6.7 per cent carcinoma in clinically benign breast lesions. The good prognosis in the group of thyroid cancers found histologically in nodules not suspected of malignancy upon physical examination is another point in favor of the early removal of all nodular goiters.

The importance of both surgical and radiotherapeutic methods in the treatment of thyroid cancer is generally recognized. Surgical removal, in the case of operable tumors, is usually the initial treatment and there are many cases of carcinoma of the thyroid in which the indications for treatment by some form of radiation are clear-cut and beyond dispute. On the other hand, the value of routine postoperative irradiation for thyroid cancer is not a matter of general agreement. Lahey, Hare and Warren<sup>13</sup> recommend postoperative radiotherapy for all carcinomas of the thyroid, regardless of the pathologic type or extent of the tumor, whereas Portmann<sup>17</sup> considers that such routine treatment is of no benefit in those cases in which the diagnosis of carcinoma was made only after microscopic examination of the excised thyroid tissue, and of questionable benefit in those cases in which the tumor, although suspected clinically, remained confined within its capsule.

It is in an attempt to evaluate our experience with thyroid cancer, and especially to determine as far as possible the indications for postoperative radiotherapy, that we have reviewed the cases of carcinoma of the thyroid treated in the Hospital of the University of Pennsylvania since July, 1933.

## INCIDENCE

During the period from July 1, 1933 to December 31, 1944, 2,079 lesions of the thyroid have been observed in the Laboratory of Surgical Pathology of the Hospital of the University of Pennsylvania. These have been classified in Table I.

# CARCINOMA OF THYROID

If the 944 toxic and nontoxic diffuse goiters included in this series are eliminated from the computations, the incidence (among nodular thyroid enlargements) of adenoma becomes 10.1 per cent, of papillary cystadenoma

TABLE I

	Number	Per Cent
Diffuse toxic goiter	923	44.4
Diffuse nontoxic goiter	21	1.0
Nodular nontoxic goiter	637	30.6
Nodular toxic goiter	279	13.4
Chronic thyroiditis	30	1.4
Tuberculosis	1	0.1
Adenoma	115	5.5
Papillary cystadenoma	11	0.5
Carcinoma	62	3.0
Total	2,079	99.9

10 per cent and of carcinoma 5.5 per cent. These figures for the incidence of carcinoma—3.0 per cent of all surgically treated goiters (2,079) and 5.5 per cent of surgically treated *nodular* goiters (1,135)—are comparable to those of Ward,<sup>21</sup> whose figures, based on a considerably larger series than ours, are 3 per cent and 4.8 per cent, respectively. Cole, Slaughter and Rossiter<sup>3</sup> report that 7.2 per cent of the 523 nodular goiters they observed were malignant, and Stout<sup>20</sup> reports that 2.5 per cent of the 4,671 goiters of all types treated surgically at the Presbyterian Hospital in New York between 1924 and 1944 were malignant. Brenizer and McKnight<sup>1</sup> noted an incidence of carcinoma of 4 per cent in 2,324 patients with nodular goiters.

In the series of cases of thyroid carcinoma which we have analyzed we have included, in addition to the 62 cases noted above, five patients who had no surgical treatment but on whom autopsy material is available, three patients, also dead, on whom no pathologic material is available but whose clinical courses leave little doubt as to the diagnosis (all had roentgenographic evidences of metastases) and one case in which a pathologic diagnosis was made elsewhere and confirmed in this laboratory but in which the material is no longer available and cannot be reviewed for pathologic classification (Table II).

TABLE II

CASES OF THYROID CARCINOMA OBSERVED AT THE  
HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA

July 1, 1933—December 31, 1944

Cases treated surgically (HUP)	62	
Autopsied cases (no surgical treatment)	5	
Total cases in which pathologic material is available		67
Cases treated surgically elsewhere (pathologic diagnosis made but material not now available)	1	
Cases diagnosed clinically (with roentgenographic evidence of metastases)	3	
Total cases		71

We have excluded several patients diagnosed clinically as having carcinoma of the thyroid but who died or were lost from follow-up with evidences of local disease only and who, therefore, may have had chronic thyroiditis rather than

neoplasm Such exclusions are more or less balanced by the exclusion of several living patients who possibly, or probably, had malignant thyroid lesions but with regard to whom the clinical data are insufficient or the pathologic material inadequate to assure us of the diagnosis During this 11 5-year period, then, 71 cases of carcinoma of the thyroid have been observed and treated in the Hospital of the University of Pennsylvania

#### AGE

Seventy per cent of this series of thyroid carcinomas were recognized in patients between the ages of 41 and 70, an age-incidence very similar to that reported by Ward<sup>21</sup> Our series includes one patient 19 years old, and 17 between the ages of 25 and 40 years Although it is not apparent in our material, the occurrence of thyroid cancer in childhood is well known<sup>8, 15</sup>

Portmann<sup>17</sup> has classified thyroid carcinomas according to the extent of the disease as follows

GROUP I—Cases without clinical evidence of malignant tumors of the thyroid gland, the neoplasms being small and discovered only after microscopic examination of tissues removed

GROUP II—Cases without clinical evidences of malignant tumors of the thyroid gland or their presence suspected only on the basis of the age of patients and recent rapid enlargements of goiters of long-standing, or discovered at operation or microscopic examination and the tumors still localized within the capsule of the glands

GROUP III—Cases with clinical or pathologic evidences of malignant tumors of the thyroid gland which had invaded or extended outside of the capsules of the thyroid glands but without clinical or roentgenologic evidences of metastases

GROUP IV—Cases with clinical or pathologic evidences of malignant tumors of the thyroid gland and also clinical or roentgenologic evidences of metastases

TABLE III  
AGE DISTRIBUTION OF PATIENTS WITH THYROID CARCINOMAS  
(CLASSIFIED ACCORDING TO PORTMANN'S METHOD)

Portmann's Group	Total No Pts	No Pts under 50 Yrs of Age	Per Cent
I	27	19	70
II	5	4	80
III	23	7	30
IV	15	6	40
	<hr/>	<hr/>	<hr/>
Total	70*	37	53

\* The clinical data are insufficient to classify one patient according to this method

Classification of the present series by this method (Table III) brings out the interesting observation that 70 per cent of the patients in Groups I and II were less than 50 years old, whereas, of the patients in Groups III and IV, only 34 per cent were under 50 years of age, when they first came under our observation

SEX

Fifty-four, or 76 per cent, of the patients in our series were women, a ratio of approximately three females to one male. Ward<sup>21</sup> reports a sex ratio of one man to three or four women for malignant goiter and he, as well as Cole, and his associates,<sup>3</sup> and others, note even greater preponderance of other thyroid lesions in the female sex.

THYROTOXICOSIS

Of this group of 71 patients with thyroid carcinoma, two (3 per cent) showed unequivocal evidences of hyperthyroidism and in four others there was less definite, or questionable, evidence of thyrotoxicosis. Although carcinoma is rare in toxic diffuse goiter (Ward<sup>21</sup> encountered only one carcinoma in 1900 toxic diffuse goiters, and Cole and his associates<sup>3</sup> one in 435 cases), the association of clinical manifestations of thyrotoxicosis with malignant lesions of the thyroid is not uncommon and has been reported to occur in as high as 33.5 per cent of a series of 245 cases of thyroid carcinoma by Pemberton and Lovelace.<sup>15</sup> Goetsch<sup>5</sup> has described nine carcinomas in diffusely hyperplastic goiters. One of our unquestionably toxic patients died as a result of the carcinoma, the other whose carcinoma was small, and an incidental pathologic finding, is alive and well more than nine years after surgical excision.

RELATIONSHIP OF CARCINOMA TO NODULAR GOITER AND ADENOMA

Cole, and his co-authors<sup>3</sup> have emphasized the frequency with which nodular goiters may become malignant. Eleven per cent of the 100 nontoxic multinodular goiters in their series were identified as carcinomas, and no less than 24 per cent of the solitary nontoxic nodules were malignant. Lahey, Hare and Warren believe that 80-90 per cent of thyroid tumors arise from preexisting adenomas, a conclusion with which most writers are essentially in agreement. Lahey,<sup>14</sup> and Warren<sup>22</sup> also emphasize the frequency with which the solitary nodule proves to be malignant. There is ample evidence that a large proportion of the carcinomas in our series had their origin in preexisting benign tumors, but in many cases our material and data are not sufficiently complete to permit us to reach any definite opinion on this point. However, 74 per cent of the patients in this series gave a history of a preexisting goiter of at least one year's duration and 42 per cent had a history of a goiter of at least five years' duration. Many of the goiters had been present for 10 to 15 years, or longer, and three for more than 35 years. The history of preexisting goiter was most striking in the cases of Group I (Portmann's classification), all of which had a history of a goiter of at least one year's duration and 69 per cent of which had had a goiter for five years, or more.

PATHOLOGIC CLASSIFICATION

The pathologic classification we have used is essentially that proposed by Warren.<sup>23</sup> However, we have frequently found it difficult or impossible to distinguish between malignant papillary cystadenoma and papillary adenocarci-

noma and, therefore, placed all the papillary tumors in a single group and listed them, along with the malignant adenomas, as tumors of low or potential malignancy. With regard to this point, it is of interest that Lahey, Hare and Warren<sup>13</sup> report a higher incidence of five-year survivals (80 per cent) for papillary adenocarcinomas, which they consider to be of an intermediate grade of malignancy, than for the potentially malignant papillary cystadenomas with blood vessel invasion (62 per cent). Ward<sup>21</sup> classifies the malignant adenoma as of a higher grade of malignancy than the papillary carcinoma. The classification of the 67 cases in our series on which pathologic material is available is given in Table IV. We have followed Stout<sup>20</sup> in grouping the Hurthle cell carcinoma with the less malignant tumors, especially since the single case of this type in our series was a clinically unsuspected, encapsulated tumor which did, however, show intravascular growth.

TABLE IV

	Number	Per Cent
1 Low degree of malignancy	41	61.5
Malignant adenoma	20	30
Papillary carcinoma	20	30
Hurthle cell carcinoma	1	1.5
11 Moderate degree of malignancy		
Adenocarcinoma	18	27
111 High degree of malignancy	8	11.5
Small cell carcinoma	1	1.5
Giant cell (and spindle cell) carcinoma	7	10

In the case of tumors showing a variable histologic picture, we have classified them according to the predominant type of growth (Fig. 1). The relative numbers of each type show a distribution not very different from that reported by Cole, and his associates,<sup>3</sup> and by Stout.<sup>20</sup> We did not encounter any squamous cell tumors in this study. Although small areas of squamous cell differentiation were present in several of our carcinomas, this type of tissue did not predominate in any case. Two of the tumors in this series were composed almost entirely of spindle-shaped cells. Both showed areas indicating their carcinomatous nature, and in one case there were colloid-containing follicles in a uterine metastasis.<sup>19</sup>

#### METASTASIS

Metastases occurred in 25 of these 71 patients. There were 33 different sites of involvement, the most frequent being the cervical lymph nodes (11 times), bones (nine times) and lungs (six times). The liver, cerebrium and mediastinal nodes were each involved twice and the uterus once. Multiple metastases were especially noteworthy in the cases with bone lesions, one patient showing widespread involvement of the entire osseous system. The femur was involved in four instances, the bones of the skull and pelvis each in three instances and the sacrum twice. Single cases showed metastases in the thoracic and lumbar spine, rib, humerus, radius and mandible.

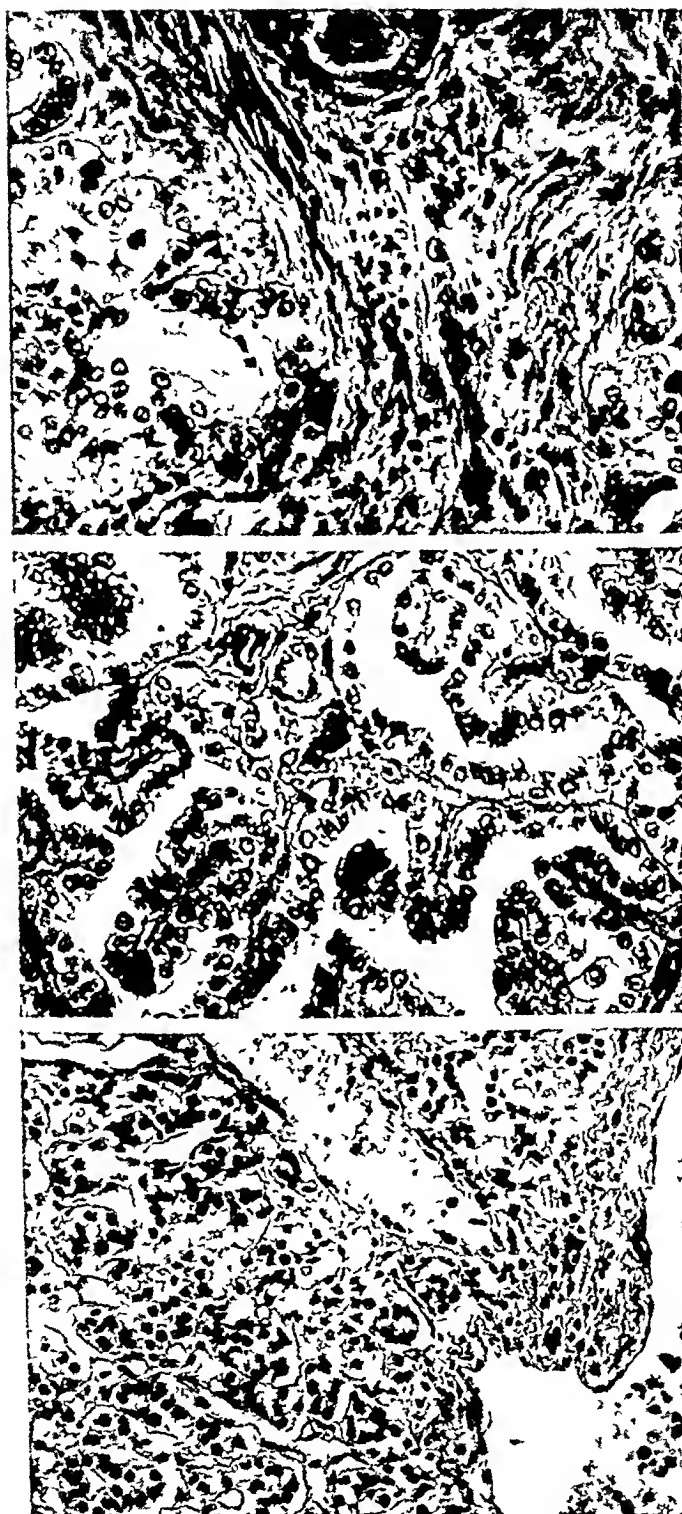


Fig 1—(A) Carcinoma of thyroid of malignant adenoma type (with blood vessel invasion)  
(B) Papillary carcinoma of thyroid  
(C) Adenocarcinoma of thyroid



## BLOOD VESSEL INVASION

Definite histologic evidence of blood vessel invasion was encountered in 36 (54 per cent) of 67 cases. We have not found intravascular growth to be of significance in the prognosis of thyroid cancer. Twenty-four of the cases in which this finding was present have been followed for three years, or more, and 11 of them are without symptoms, and have survived for periods of from three to 12 years. On the other hand, as originally pointed out by Graham,<sup>6</sup> blood vessel invasion is an extremely useful and important diagnostic criterion. Its importance is greatest in the adenoma malignum group, where the diagnosis of malignancy must not infrequently rest largely, or wholly, upon the basis of this finding.<sup>13</sup>

## RESULTS OF TREATMENT

There is general agreement in the literature upon surgical removal as the initial treatment of choice in thyroid cancer. Indeed, as already pointed out, the diagnosis is frequently unsuspected until after surgery has been performed. There is similar general agreement upon the efficacy of radiation therapy, especially for papillary tumors.<sup>7, 9, 16, 17, 18, 23</sup> Lahey, Hare and Warren<sup>17</sup> recommend postoperative radiation in all cases in which a diagnosis of carcinoma is made, regardless of the type or extent of the tumor.

Our series includes several cases in which surgical removal of a carcinoma of the thyroid was known to be incomplete, but in which the disease has been arrested by radiation therapy, and the patients have survived without symptoms over long periods of time. One such patient is alive and well 7 1/2 years after incomplete removal of an adenocarcinoma, another is alive and without symptoms eight years after simple biopsy of a papillary carcinoma. A number of other patients have survived for 2 to 4 years following incomplete extirpation or biopsy and irradiation. Some of the patients in this last group have subsequently died, but several are alive and are asymptomatic.

It must be remembered, however, that, in cancer of the thyroid in particular, we must be cautious in speaking of "cures," since many patients remain well for five, or more, years following the diagnosis of carcinoma and the initial treatment only to succumb later with extension of the malignant disease. Our series includes one patient who developed a metastasis in the humerus after eight asymptomatic years following thyroidectomy for an adenocarcinoma. Her arm was amputated, and she remained well for another three years before developing multiple bone metastases. This patient was a "ten-year survival" although she eventually died as a result of her thyroid carcinoma.

Nevertheless, in the light of our experience, there can be no doubt of the value of roentgenotherapy, even though we may never be assured of permanent cures by this means. Among the patients we have studied there is one who had a small cell carcinoma (Fig 2), and who is alive and well ten years after surgical removal and irradiation, and one patient with a giant cell carcinoma (Fig 3) who survives ten years after partial surgical removal and postoperative roentgenotherapy. Both of these patients had tumors of a pathologic type

which Ward<sup>21</sup> considers hopeless. We have briefly noted instances of favorable results in cases of four different pathologic types, but it should be added that our experience is in agreement with that of others in that the papillary carcinomas appear to be more radiosensitive than other types.

In Table V our five- and ten-year survivals are listed according to the pathologic classification of the tumors. Table VI lists the survivals according to Portmann's<sup>17</sup> classification. In each table the survivals — those patients known to be living and without symptoms—have been computed on the basis of the total number of patients treated more than five (or ten, as the case may be) years ago.

TABLE V  
FIVE- AND TEN-YEAR SURVIVALS ACCORDING TO PATHOLOGIC CLASSIFICATION

Type of Tumor	No of Pts Treated more than 5 Yrs ago	5-Yr Survivals		No of Pts Treated more than 10 Yrs ago	10-Yr Survivals	
		No	Per Cent		No	Per Cent
Malignant adenoma	13	7	54	4	2	50
Papillary carcinoma	11	7	64	6	4	67
Malignant adenoma and papillary ca (together)	24	14	58	10	6	60
Adenocarcinoma	12	6	50	6	3	50
Small cell carcinoma	1	1	100	1	1	100
Giant cell carcinoma (incl spindle cell ca.)	5	2	40	2	1	50
Small cell and giant cell carcinoma (together)	6	3	50	3	2	67
Totals	42	23	55	19	11	58

TABLE VI  
FIVE AND TEN YEAR SURVIVALS (ACCORDING TO PORTMANN'S CLASSIFICATION)

Group	No of Pts Treated more than 5 Yrs ago	5-Yr Survivals		No of Pts Treated more than 10 Yrs ago	10-Yr Survivals	
		No	Per Cent		No	Per Cent
I	14	12*	86	8	6*	75
II	3	2	67	1	1	100
III	17	7	41	8	4	50
IV	9	2	22	3	0	0
Unclassified	1	0	0	—	—	—
Totals	44†	23	52	20‡	11	55

\* Only one death among the patients in GROUP I is attributable to the thyroid carcinoma.

† 41 of these 44 patients have been followed. Two patients are included, on whom pathologic material is not available.

‡ 19 of these 20 patients have been followed. One patient is included, on whom pathologic material is not available.

In our experience, as presented in Table V, the pathologic classification of a thyroid carcinoma has a limited bearing on the prognosis. On the other hand, the end-results in the early cases (GROUPS I and II—Portmann) are strikingly better than in the more advanced cases (GROUPS III and IV—Portmann), regardless of tumor type (Table VI). It should be noted, however, that the

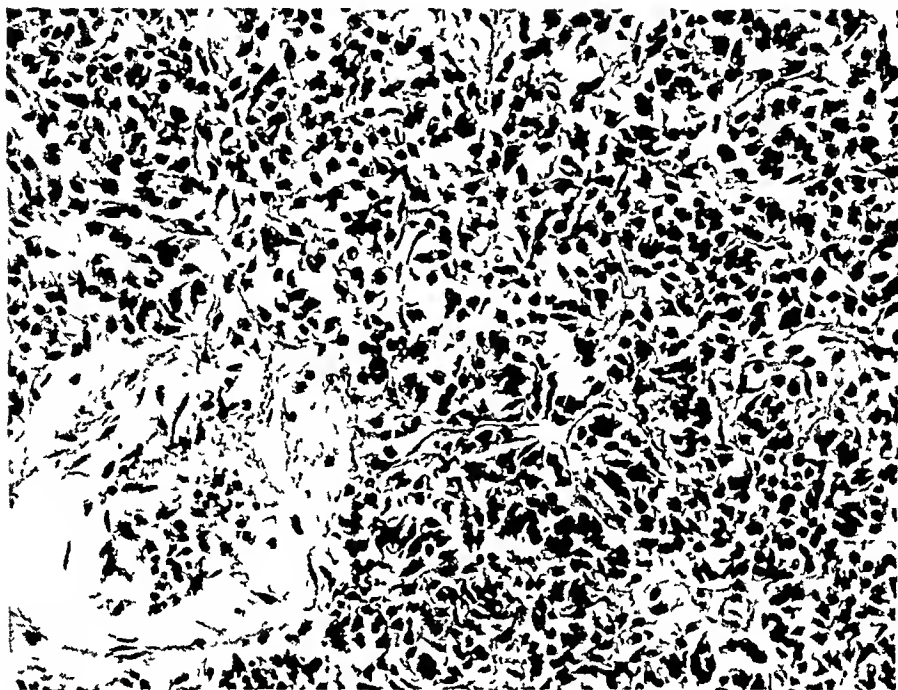


FIG 2—Small cell carcinoma of thyroid The patient, a 19-year-old male, is alive and well, ten years after surgical removal and postoperative radiation

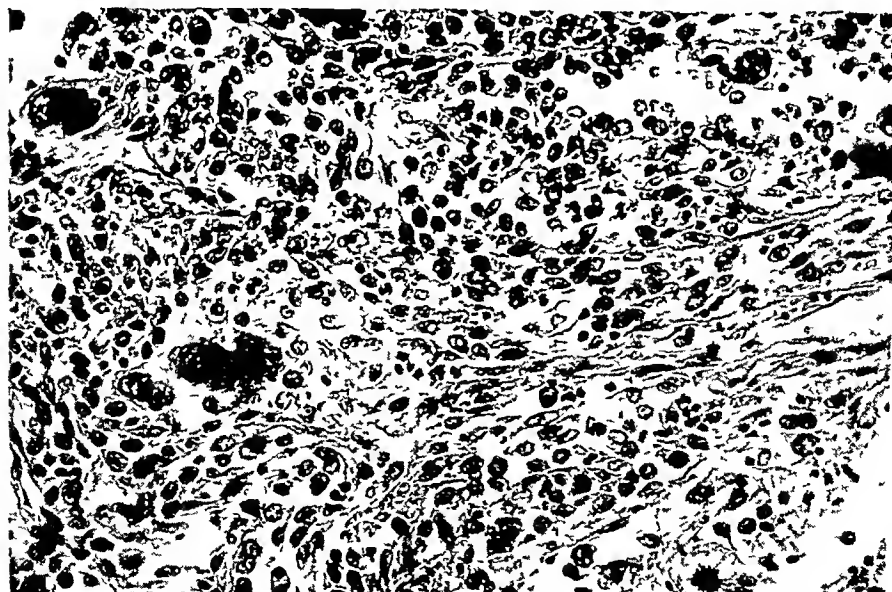


FIG 3—Giant cell carcinoma of thyroid The patient, a 54-year-old female, is alive and well, ten years after surgical removal and postoperative radiation

last two groups include a significantly greater number of patients over 50 years of age than do the first two groups (Table III) and that, therefore, the patients in Groups III and IV have a shorter life-expectancy regardless of the advanced state of their thyroid carcinomas.

Among the deaths occurring in GROUP I cases, only one could be attributed directly to the thyroid carcinoma. One patient with a malignant adenoma died after four years with an independent primary carcinoma of the gallbladder, one with an adenocarcinoma after six years of a "stroke", and the third, who had a papillary carcinoma, after nine years with a large gastric ulcer and renal decompensation. At the time of death none of these three patients had evidence of recurrence or metastasis of the thyroid carcinoma. One patient is alive, with metastases seven and one-half years after operation. At five years she had been asymptomatic.

Many authors, notably Ward<sup>11</sup> and Portmann,<sup>17</sup> among those who recently have written on the subject, have emphasized the tremendous importance of the extent of the disease in determining the prognosis. The experience of Rosh and Raeder,<sup>18</sup> as well as our own, further supports this view.

#### POSTOPERATIVE RADIATION

Approximately one-half of the patients in GROUP I (Portmann,<sup>17</sup> Table VII) received postoperative radiation, whereas almost all of those in the other groups were so treated. Exceptions among the latter were, for the most part, patients who died before treatment could be instituted or before more than minimal amounts of radiation could be administered. The series, exclusive of the cases in GROUP I, includes 11 five-year survivals and five ten-year survivals. All but one of these patients received radiation. Our series does not include an adequate group of patients in Portmann's Groups II, III and IV who did not receive radiation to be used as a control series. In view of the character and extent of the lesions in these patients, the results obtained with operation and radiation were much better than had been anticipated. The prolonged survival of certain patients in whom the carcinoma could not be entirely removed, as judged grossly, leaves little doubt of the effectiveness of radiation.

TABLE VII  
COMPARISON OF THE GROUP I SURVIVALS WITH AND WITHOUT RADIATION

	No of Pts Treated more than 5 Yrs ago			No of Pts Treated more than 10 Yrs ago		
	5 Yr Survivals			10-Yr Survivals		
	No	Per Cent		No	Per Cent	
With radiation therapy	7	100		5	80	
Without radiation therapy	7	71		3	67	

The patients in GROUP I include three who died of unrelated conditions, without evidence of recurrence or metastasis of the thyroid tumor and one nonirradiated patient (not counted as a survival) who has been lost to follow-up. Thus, this group included only one case who is known to have died of

thyroid carcinoma within ten years. This patient was treated postoperatively by irradiation, but it is to be noted that her tumor was of the highly malignant spindle cell type.

In addition, one patient who survived ten years subsequently died with metastases, and another patient has developed a metastasis in the sacrum after seven and one-half years of freedom from clinical evidence of disease. Neither of these two patients received roentgenotherapy.

When one takes the pathologic classification into consideration, comparisons between radiated and nonradiated cases are possible only with the least malignant types. Our series includes nine five-year survivals and five ten-year survivals among patients with tumors classified as adenocarcinomas or giant cell, small cell or spindle cell carcinomas, but all of these patients were radiated, with the single exception of the ten-year survival, already mentioned, who subsequently succumbed to her disease. Table VIII compares the results with and without roentgenotherapy in the papillary carcinomas and malignant adenomas.

TABLE VIII  
THYROID CARCINOMAS OF LOW OR POTENTIAL MALIGNANCY

	No of Pts Treated more than 5 Yrs ago	5 Yr Survivals		No of Pts Treated more than 10 Yrs ago	10 Yr Survivals	
		No	Per Cent		No	Per Cent
Malignant Adenomas						
With radiation therapy	8	4	50	2	1	50
Without radiation therapy	5	3	60	2	1	50
Papillary Carcinoma						
With radiation therapy	6	5	83	4	3	75
Without radiation therapy	5	2	40	2	1	50
Total						
With radiation therapy	14	9	64	6	4	67
Without radiation therapy	10	5	40	4	2	50

TABLE IX  
THYROID CARCINOMAS OF INTERMEDIATE AND HIGH DEGREES OF MALIGNANCY

	No of Pts Treated more than 5 Yrs ago	5-Yr Survivals		No of Pts Treated more than 10 Yrs ago	10 Yr Survivals	
		No	Per Cent		No	Per Cent
With radiation therapy	17	9	53	8	4	50
Without radiation therapy	3	1	33	2	1	50

The figures in Table VIII suggest that benefit is more likely to be obtained from radiotherapy in the papillary carcinomas than in other types, a point which is in agreement with general experience of others.

Table IX compares the results with and without radiation in the more malignant tumors. The differences are not statistically significant. The number of cases is small, and it must also be remembered that the advanced cases with a poor, or hopeless, prognosis were usually given roentgenotherapy.

These data support the opinion of Portmann that routine postoperative roentgenotherapy does not clearly benefit the patient with a malignant adenoma or papillary carcinoma of the thyroid which has been discovered only on pathologic examination and which is confined within a capsule. However, our clinical observations lead us to believe that all other cases should receive radiation therapy.

#### LATERAL ABERRANT THYROID

During the 115 years covered by this report we have encountered four lateral aberrant thyroid tumors. The subject of lateral thyroid tumors has been thoroughly discussed by Fiantz, and her associates,<sup>4</sup> and by Clay and

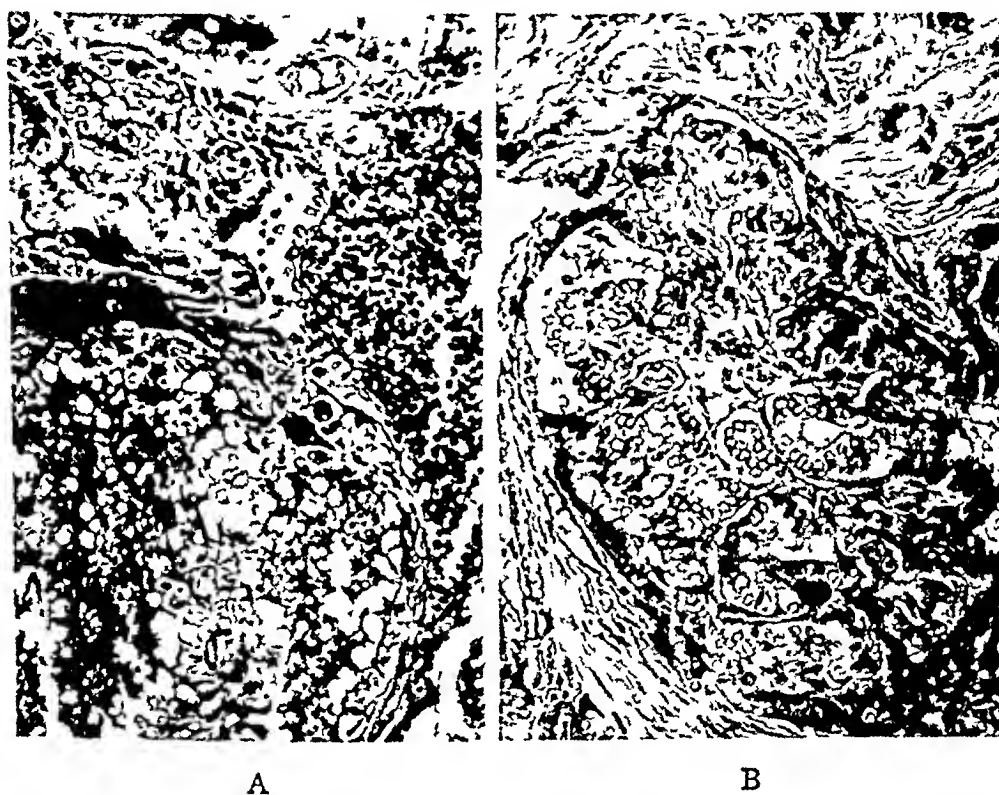


FIG 4—(A) Papillary carcinoma of lateral aberrant thyroid  
(B) Carcinoma of the main thyroid gland of same patient, a 22-year-old male

Blackman.<sup>2</sup> One of the lateral thyroid lesions in our series was benign but the other three were malignant, and all were predominantly papillary, with multiple lateral cervical nodules. The three patients with carcinoma were all males, age 19, 22 and 39, respectively. All are living without symptoms following surgical removal and roentgenotherapy, but they have all been treated within the past three years.

One patient in this group was the subject of radical neck dissection, during the course of which the homolateral lobe of the thyroid gland was resected. The operating surgeon (J. E. R.) was not aware of any suspicious lesion in the lobe but, nevertheless, a small carcinoma was detected on pathologic examination (Fig 4). The main thyroid glands of the other two patients have not been removed, or explored, surgically, but neither patient presents clinical

evidence of involvement of the main gland as yet. Clay and Blackman<sup>2</sup> believe that the so-called lateral thyroid tumors are all metastases from occult carcinomas of main thyroid gland. Frantz, and her associates,<sup>1</sup> on the other hand, are convinced of the origin of these tumors in aberrant thyroid tissue, despite a frequent association with carcinoma in the main gland, which they consider to be independent. Our experience with these lesions is too small to permit us to draw any conclusions on this point but, since collecting this series, we have observed two additional patients with multiple, malignant lateral cervical thyroid tumors. Although the thyroid glands of these patients appeared normal at surgical exploration lobectomies were performed, and small carcinomas were found in both cases. This limited experience lends some support to the contention of Clay and Blackman,<sup>2</sup> and of King and Pemberton,<sup>12</sup> that the so-called lateral aberrant thyroid carcinomas are, in reality, metastases from tumors of the thyroid gland.

The two patients who have not had thyroidectomies have done well. Both have had roentgenotherapy. The follow-up is still much too short to permit of accurate evaluation. In the case of the 19-year-old boy, the tumor was considered inoperable at a second operation for removal of recurrent or newly-developing nodules. Following intensive radiation, however, surgical removal was readily accomplished at a later procedure. The 39-year-old patient had a somewhat similar experience. He developed new or recurrent nodules within five months of the operative removal of the tumor observed originally. These were very extensive and complete removal was impossible. Following radiation this patient has remained without clinical evidence of thyroid or lateral thyroid disease for three and one-half years.

#### RADIOLOGIC CONSIDERATIONS

Fifty-two of the 71 patients in this group received radiation therapy. The records of 50 are complete with respect to technical factors and dosage.

Although the treatment was modified to meet individual requirements, most of the patients were treated at 200kv, 15ma, 0.5 mm of copper and 1 mm of aluminum filtration added, and 50 cm TSD. Three portals were commonly directed to the neck, each lateral and an anterior portal, with a posterior portal sometimes added. The portals usually measured 10 x 13 cm or 15 x 16 cm.

Most of the patients were given from 1,500 to 2,000 air roentgens to each portal in daily amounts of 200 air roentgens to one or two portals. The average total dose to the neck was about 5,000 air roentgens. Larger doses were given in several series. At present, our policy is to wait at least 2 to 3 months following surgery before beginning radiation therapy in order to permit physiologic repair to take place. If the surgical procedure is limited to a simple exploration and biopsy, irradiation is instituted immediately.

The average total dose to the neck among those patients who have survived five years, or more, was about 6,000 air roentgens. The smallest dose in this group of five-year survivors was 4,896 air roentgens.

In the group of lateral aberrant thyroid carcinomas, all three have received radiation therapy. Similar technical factors to those above were employed and the total dosage was 2,000 to 3,000 air roentgens to each of two or three portals.

Two patients with bony metastases were treated over the involved areas, and one showed recalcification of the lesion after 1,000 to 1,500 air roentgens had been given to two portals, while the other showed no recalcification after 1,000 to 2,500 air roentgens had been given to three portals. One patient with pulmonary metastases showed definite clinical and roentgenographic evidence of improvement after 1,200 to 1,600 air roentgens to anterior and posterior portals, respectively.

Our dosage to the primary tumor is quite similar to that of Hare's<sup>8</sup> who attempts to give 6,000 air roentgens to the tumor bed. This amount, he believes, is close to the lethal tumor dose. He, however, begins therapy five or six days after operation because he has observed two cases who developed evidence of recurrence within two weeks after operation.

In none of our patients has there been any delay in wound healing. Mucositis usually developed after 12 to 14 days of treatment. The external skin reaction reached a maximum after about a month.

One of our patients presented an interesting problem in the management of pulmonary metastases. The roentgenologic examination of the chest revealed increased prominence of the lymph nodes in each hilum and an increase of the prominence of the lung markings in the right upper lobe, which was regarded as evidence of metastasis. Approximately 4,000 air roentgens were given to each of four portals directed toward the mediastinum. This resulted in a tissue dose of 3,698r to the center of each lung. Two months later the patient returned with dyspnea and cough following a cold. A roentgenogram at this time showed bilateral pneumonitis, and the possibility of radiation pneumonitis was considered. The patient's course continued downhill in spite of medical measures to combat infection, and he died. At autopsy, in addition to metastatic involvement of the hilar lymph nodes, a very firm infiltration of the right upper and left lower lobes was found. Histologic examination revealed radiation pneumonitis and metastatic carcinoma. We believe that the presence of metastatic carcinoma in this patient's lungs rendered him especially susceptible to radiation pneumonitis, and we would advise treating such patients with extreme caution.

#### SUMMARY AND CONCLUSIONS

Seventy-one cases of carcinoma of the thyroid and three of lateral thyroid carcinoma treated at the Hospital of the University of Pennsylvania during an 11 1/2-year period have been reviewed. Sixty-two thyroid cancers were encountered among a series of 2,079 surgically-treated thyroid lesions, an incidence of 3.0 per cent. This is an incidence of 5.4 per cent of carcinoma in 1,135 surgically treated *nodular* goiters.

Although the age-incidence is not greatly different from that of carcinoma



of other organs, the thyroid carcinomas occurring in the younger age-groups tend to be of the less malignant pathologic types and to be less advanced in their growth when they first come under observation

A majority of thyroid carcinomas are of the papillary or malignant adenoma types, which may be grouped together as GRADE I tumors, or tumors of low or potential malignancy. Fifty-eight per cent of the patients treated for tumors of these types more than five years ago, and 60 per cent of those treated more than ten years ago are alive and well. Although the prognosis in tumors of other pathologic types is poorer, the ten-year survivals in our series include one patient with a small cell carcinoma and one with a giant cell carcinoma.

So far as prognosis is concerned, the extent of the disease at the time treatment is instituted is more significant than the pathologic type. Eighty-six per cent of the patients whose tumors were discovered only on pathologic examination, and who were treated more than five years ago, are alive and well. Seventy-five per cent of such patients treated more than ten years ago are alive and well.

Many patients with thyroid cancer develop metastases or recurrences five years, or more, after their initial treatment. This series includes one patient who died with metastases more than ten years after thyroidectomy.

In view of the relatively small risk of operation, it would appear wise to recommend the surgical excision of all nodular goiters unless strong contraindications exist. If carcinoma is present and extends through the capsule of the gland, postoperative radiation should be instituted. It has been especially effective in the papillary carcinomas. The benefits of postoperative radiation in cases in which the carcinoma has not extended through the capsule are not clear from the present study. So many of these patients do well that a considerably greater experience will be required before postoperative radiation in this group of cases can be finally evaluated.

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# PRIMARY CARCINOMA OF THE LUNG, WITH INVASION OF THE RIBS

PNEUMONECTOMY AND SIMULTANEOUS BLOCK RESECTION OF THE CHEST WALL

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CLINICAL REPORTS have directed little attention to the incidence, behavior and treatment of carcinoma of the lung invading the bony thorax and such extension has been accepted generally as a contraindication to curative surgical attempts<sup>2, 3, 9, 11</sup>. The purpose of this communication is to question the relegation of these patients to an incurable group and to emphasize a method of treatment based upon sound principles of cancer surgery.

The incidence of bony thorax invasion is probably between five and ten per cent of all patients with carcinoma of the lung. Pathologic studies<sup>5, 6, 7</sup> have not only pointed out the frequency of chest wall invasion, but have emphasized the behavior of the cell type in relationship to rib erosion. In Koletsky's<sup>5</sup> study, five, or 8.3 per cent, of the 40 patients with squamous cell carcinoma of the lung showed an associated rib destruction, and this observation was confined to this cell type. A histologic diagnosis of primary cancer of the lung was made in 88 consecutive cases during the past eight years by the author. Seven patients, or 8 per cent, showed invasion of the chest wall, characterized by rib destruction in six cases.

The relationship of the cell type of carcinoma of the lung to erosion of the ribs or vertebrae is striking, however, there is a paucity of literature in attempting to confirm this correlation. The majority of so-called Pancoast<sup>8</sup> tumors are carcinomas of the lung. These tumors have as one clinical feature the local and adjacent destruction of a rib, and it was of interest to review the cell types of some of the published cases. Stein<sup>10</sup> reported 27 cases of malignant lesions in the region of the pulmonary apex, so-called superior pulmonary sulcus tumors. In nine bronchogenic carcinomas in which the cell type was determined, six were of the squamous cell variety and three were classified as adenocarcinomas. Haben and Miller<sup>4</sup> were able to collect, in 1938, a series of 27 reported cases fulfilling the requirements for a diagnosis of a Pancoast tumor. The cell type was given in 19 tumors, and in 14, where the bronchogenic origin seemed most probable, the squamous cell variety accounted for ten, adenocarcinoma two, medullary carcinoma one, and undifferentiated carcinoma one. Five of the 100 patients with carcinoma of the lung studied at autopsy by Koletsky<sup>5</sup> showed rib destruction, and in each instance the squamous cell type of tumor was present. In my series of 88 histologically proved carcinomas of the lung, the incidence of the squamous cell variety was 47 per cent, adenocarcinoma 24.1 per cent, and small cell carcinoma 28.9 per cent. The cell type was unclassified in five cases. The six cases showing invasion and destruction of a rib or ribs were of the squamous cell type. One

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adenocarcinoma showed pericostal invasion of the soft tissue of the chest wall, but there was no osseous extension of the tumor. In our study of cases, 15.4 per cent of the squamous cell variety of lung cancer invaded the ribs, and this behavior was limited to this cell type. Squamous cell carcinomas of peripheral bronchogenic origin constitute the majority of primary lung tumors characterized by invasion of the chest wall with rib destruction.

The behavior of peripheral squamous cell carcinomas is not unlike the more centrally placed tumors of this type. This variety of tumor invades contiguous structures, infiltrates, grows slowly and metastasizes late in the course of the disease. In 100 postmortem examinations, Koletsky<sup>5</sup> found no extrathoracic dissemination in 65 per cent of the 40 cases with the squamous cell type. Olson<sup>7</sup> found regional node metastasis in 55 per cent and no nodal involvement in 14 per cent of 27 squamous cell carcinomas studied at autopsy. The behavior of this cell type is well-appreciated clinically. Thirteen of the 14 surviving patients in Adams<sup>1</sup> series of 49 pulmonary resections belong to the squamous cell group. In my series of 88 patients with carcinoma of the lung, it was possible to undertake a curative resection in 17, and of this group eight were of the squamous cell variety.

Although extension of carcinoma of the lung to the bony thorax is indicative of a well-advanced lesion, it is not indicative of a hopeless situation. If the local lesion can be excised with a healthy margin of soft tissues and bony thorax, the prognosis is favorable. In four cases accompanied by rib destruction, Koletsky<sup>5</sup> found no metastasis to the regional nodes at autopsy. In the six patients herein reported, there was no extension to the regional nodes.

Primary carcinoma of the lung accompanied by rib destruction in the majority of instances is due to the squamous cell type of tumor. The favorable pathologic behavior of this cell type lends itself well to radical cancer surgery. This has prompted the following case reports.

### CASE REPORTS

**Case 1**—C. C., a 40-year-old white female, had an 11 months' history of pain in the right chest unaccompanied by cough or other symptoms suggesting pathology of the right lung. The pain did not radiate down the right arm but remained localized to the right side of the chest. The pain was described as being of a sharp and "tearing" character, and for two months prior to her hospital admission morphine had been used daily to alleviate this symptom. The past history did not contribute any pertinent information, and the family history was irrelevant.

*Physical Examination* The patient was having acute pain. Tenderness was present over the third rib adjacent to the spine. No other physical findings of pathology were present. The routine laboratory studies were negative. Roentgenologic examination of the thorax revealed a right apical tumor mass adjacent to the spine. The diagnostic bronchoscopy was negative and the right upper lobe orifice did not appear to be retracted upward. A diagnostic pneumothorax revealed a tumor mass involving the right upper lobe and the adjacent thoracic wall (Fig. 1). The third rib was partially destroyed adjacent to its respective transverse process.

*Operation*—February 2, 1940. A right upper lobe lobectomy was performed, removing a block of the chest wall with the specimen. Posteriorly, the second, third, fourth and fifth ribs and their respective transverse processes were divided. The neurovascular

bundles were ligated. The ribs and intercostal bundles were divided in the anterior axillary line. The tumor mass had invaded and destroyed the head of the third rib and the tip of the third transverse process. There was no metastasis present in the mediastinal nodes.

*Pathologic Report* Squamous cell carcinoma of the lung with osseous invasion of the third rib and transverse process.



FIG 1—(A and B) Case 1. Routine and overexposed roentgenograms showing destruction of 3d and 4th ribs adjacent to transverse processes.

(C) Postoperative roentgenogram showing upper lobe lobectomy and block excision of chest wall.

*Postoperative and Late Course* On the 21st postoperative day this patient was discharged from the hospital, after an uneventful convalescence. She was entirely symptom-free for a period of eight months. At this time the patient complained of pain in the region of the third dorsal vertebra and one month later a paraplegia developed at this level. She grew progressively worse and died 11 months after the pulmonary resection.

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*Autopsy* There was no evidence of metastasis to the hilar lymph nodes. There was a local extension of the tumor which could not be removed at the time of the operation. Extensive invasion of the third dorsal vertebra and spinal cord was evident.

*COMMENT* This was a palliative lobectomy, with simultaneous block resection of the chest wall. When such tumors invade the vertebrae a curative resection would appear impossible.



FIG 2—(A and B) Case 2. Routine and overexposed roentgenograms showing a large peripheral squamous cell carcinoma of the lung, with destruction of the 2d and 3d ribs. Note in (A) the clear zone between the mesial border of the tumor and mediastinum.  
(C) Routine roentgenogram of chest six years after operation.

**Case 2—J B**, a 55-year-old white male, had a nine months' history of pain in the right chest. The pain was severe in character and localized to the right infraclavicular region. Three months prior to his hospital admission he developed hemoptysis, and consulted a number of physicians relative to this complaint. During the ensuing three

months he lost 20 pounds in weight, and dyspnea became a troublesome symptom. The past history and family history were not significant.

*Physical Examination* This examination revealed all the positive findings to be limited to the chest. Deep inspiration exaggerated the pain in the right chest, which corresponded to the distribution of the third intercostal nerve. There was an inspiratory lag on the right. Tenderness over the third rib posteriorly was elicited by percussion. Dullness was present in the right scapular region and high in the right axilla. The breath sounds were decreased in these two locations. No neurologic signs were present. The routine laboratory tests were within the range of normal.

Roentgenologic examination revealed a tumor mass in the dome of the right thoracic cavity. Overexposed films showed partial destruction of the second and third ribs (Fig 2). A bronchoscopic examination revealed partial fixation of the right upper lobe bronchus. No intraluminal tumor mass was visible. Preoperative pneumothorax demonstrated fixation of the lung, tumor mass and chest wall. *Preoperative Diagnosis* Squamous cell carcinoma of the lung.

*Operation*—January 4, 1941. A right total pneumonectomy and block excision of the chest wall were carried out through a posterior approach. It was possible to cut through healthy tissue of the chest wall posteriorly and anteriorly to the tumor mass. The block of chest wall consisted of the second, third, fourth, fifth, sixth and seventh ribs and their respective intercostal bundles. The intercostal vessels were ligated close to the transverse processes and in the anterior axillary line.

The postoperative course was uncomplicated, and he was discharged from the hospital on the 25th postoperative day.

*Pathologic Report* Grade 4 squamous cell carcinoma of the lung showing invasion and partial destruction of the second, third, fourth and fifth ribs. The regional nodes showed no metastasis.

*Late Course* During the past six years, this patient has remained entirely well. There is no evidence of recurrence. He has a cough, but a recent bronchoscopic examination revealed a marked displacement of the trachea to the right and a smooth, well-healed bronchial stump. The cough appears mechanical in origin. A soft and yielding chest wall interferes somewhat with an effective cough.

**COMMENT** An extensive squamous cell bronchogenic carcinoma invading the second, third, fourth and fifth ribs, has been apparently cured by a right pneumonectomy, with simultaneous block excision of the chest wall.

**Case 3**—During the early part of December, 1942, F. P., a white male, age 41, developed pain in the right shoulder and axilla. Extraction of two teeth for apical abscesses did not relieve the pain. Six weeks of daily physical therapy seemed to exaggerate his symptoms. One month after the onset of pain, he developed a nonproductive cough, and, in March, 1943, the cough was associated with a blood-streaked sputum. One month prior to his hospital admission, he felt as if he were growing weaker, and he was somewhat short of breath. He had lost 15 pounds in weight.

*Physical Examination* He appeared chronically ill. The skin was pale and dry. The positive physical findings were limited to the chest. Tenderness was present over the right scapular region. Dullness to percussion and suppression of the breath sounds were present in this region. There were no positive neurologic findings and no evident extrathoracic extension of a possible tumor of the lung. The routine laboratory work was within normal limits. Roentgenologic examination showed the apex of the right lung to be obscured by a dense opacity measuring 6.5 cm in diameter. The mass lay posteriorly and extended into the costovertebral gutter. Overexposed films revealed partial destruction of the second rib posteriorly (Fig 3). The preoperative diagnosis was squamous cell carcinoma of the lung.

*Operation*—May 15, 1943. A posterolateral incision was made, entering the right

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pleural cavity through the seventh intercostal space. A large tumor mass replaced the apical one-half of the right lung and had invaded the second, third, fourth and fifth ribs. Resection seemed feasible, in that disarticulation of the ribs accompanied by partial resection of the transverse processes would encompass the tumor and permit block excision through healthy tissue. The first, second, third, fourth, fifth, sixth and seventh ribs were treated in this manner posteriorly and then divided in the midaxillary line. This left attached to the tumor mass and right lung the seven ribs and their respective intercostal bundles. A right pneumonectomy was then carried out. He withstood the operative procedure satisfactorily, and at no time was he in any particular danger.



FIG 3—Case 3 Overexposed roentgenogram revealing a peripheral squamous cell carcinoma of the lung, with destruction of the 2d rib

Twenty minutes after completion of the operation, the blood pressure was not obtainable in the arms. Such a marked change could not be explained on the basis of blood volume loss, for adequate blood replacement, 2,500 cc of citrated blood, had been given, however, it was soon discovered that his blood pressure was normal in his legs and absent in the arms. A marked vasospasm following trauma and dissolution of the right sympathetic trunk was then considered as a possible etiologic factor. Papaverine effected an immediate response, and the blood pressure level in the arms returned to 100/70. This return of a satisfactory blood pressure level was delayed for approximately ten minutes, for the apparent disturbing factor was not recognized. During the ensuing 32 hours, this patient temporarily regained consciousness, however, he developed intermittent generalized convulsions associated with a variable pulse rate and blood pressure



The respiratory exchange of the left lung was good. The convulsions were controlled by 25 per cent magnesium sulfate solution intravenously. The clinical picture was that of a decerebrated animal. The rectal temperature gradually rose to 108°F, and death occurred approximately 39 hours postoperatively.

*Autopsy* The specimen of lung and adherent seven ribs revealed partial destruction of the second, third, fourth and fifth ribs by a Grade 4 squamous cell carcinoma of the lung. The regional nodes removed at operation were free of metastasis.

The findings at postmortem revealed, grossly, no cause of death. The left lung was normal. There was no evidence either grossly or microscopically of residual carcinoma. Examination of the brain revealed findings compatible with cerebral asphyxia.

*Cause of Death* Encephalopathy, secondary to asphyxia.

**COMMENT** This was an advanced squamous cell carcinoma of the lung with erosion of multiple ribs, apparently curable by radical surgery. Cerebral asphyxia secondary to marked vasospasm involving the arms, neck and head seemed the most likely cause of death. A good oxygen concentration was maintained throughout the operative procedure. The photo-electric cell revealed a 90 per cent, or better, oxygenation of the blood. The ten-minute post-operative period, characterized by absent blood pressure in the arms with a normal blood pressure in the legs, was probably sufficient to produce irrevocable brain damage.

**Case 4**—T. H., a 41-year-old white male, a painter by occupation, had a history of recurrent pain in the right shoulder for a period of two years. The pain was exaggerated by damp weather and by persistent use of the right arm. Four months prior to his admission to the hospital, he developed an entirely different type of pain which was sharp, shooting and burning in character. This pain would radiate from the right shoulder to the midline of the chest. Sudden jolting movements of the right shoulder would initiate the pain in the right chest, and for two weeks he avoided use of the arm. He had no cough and no shortness of breath.

The past history revealed that he had a fracture of the left humerus in 1938, at which time he had pain in the right shoulder. His mother and paternal grandfather died of cancer. The remaining history did not contribute any findings of importance.

The physical examination was essentially negative throughout. He was a fairly well-nourished man of small stature. The routine laboratory studies were negative.

Roentgenologic examination revealed a circumscribed area of increased density in the middle one-half of the right apical and subapical region of the lung. The total area of involvement measured six centimeters in diameter. In the lateral view there was a circumscribed shadow of slightly increased density in the mediastinal region measuring three centimeters in diameter (Fig. 4). This produced a wedge-shaped density quite characteristic of a lobular atelectasis. Bronchoscopic examination was negative and there were no secretions arising from the right upper lobe orifice.

*Clinical Diagnosis* Bronchogenic carcinoma of the upper lobe of the right lung.

*Operation*—February 2, 1943. A total pneumonectomy was carried out on the right for a carcinoma involving the apex of the right lung and infiltrating the soft tissue of the chest wall. A frozen-section diagnosis of the soft tissue removed from the third interspace confirmed the clinical suspicion of invasion of the chest wall. Following removal of the right lung, a block resection of the chest wall was carried out removing the second, third, fourth, fifth and sixth ribs. The intercostal bundles were ligated adjacent to the transverse processes posteriorly, and anteriorly the bundles were divided in the anterior axillary line.

The pathologist reported bronchogenic adenocarcinoma of the lung, Grade 3, upper lobe bronchus right lung, with soft tissue extension to the chest wall. The regional nodes were not involved by metastasis.

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The postoperative course was uneventful, with the exception of the development of a small residual empyema which was drained on March 4, 1943. The empyema cavity was unaccompanied by opening of the bronchus and rapidly decreased in size. Six weeks after drainage of the empyema, he returned to his home. He has been unable to return for follow-up examination.



FIG 4—(A and B) Case 4. Routine PA and lateral roentgenograms of chest showing an apical tumor. Note the triangular area of atelectasis in the lateral film. (C) Routine roentgenogram six months after right total pneumonectomy and block excision of the chest wall.

**COMMENT** This was an advanced adenocarcinoma of the right lung invading the soft tissue of the chest wall, unaccompanied by regional lymph node involvement. There was no associated rib destruction in spite of soft tissue involvement of the chest wall adjacent to the ribs.

**Case 5**—T J was a colored male, age 42, who had a history of severe pain in the right shoulder and right side of the neck for a period of eight months. He had taken numerous drugs for the relief of pain without benefit, and two weeks prior to his admission to the hospital, the pain began to run down the inner aspect of the arm. He had been placed on morphine for the relief of pain. He had a cough for five months and a three months' history of repeated attacks of hemoptysis.

*Physical Examination* The patient was undernourished, dehydrated, and in acute pain. There was ptosis of the right lid and myosis of the right pupil. There was an absence of sweating over the right side of the face. In the right supraclavicular region there was a mass measuring 1 x 2 cm in diameter. This mass was freely movable and firm. The right arm was held close to the trunk and there was marked limitation of movement of the right shoulder. The pain radiated primarily down the inner aspect of the arm on motion. Tenderness was present over the suprascapular region on the right corresponding to approximately the first and second ribs posteriorly. Deep inspiratory movements exaggerated the pain in the right arm. There was a slight respiratory lag on the right. The percussion note was negative. The breath sounds were decreased in the right scapular region. The routine laboratory work was negative.

Roentgenologic examination revealed a tumor, measuring 4 x 6 cm, in the apex of the right lung adjacent to the spine. Overexposed films revealed destruction of the first and second ribs. Bronchoscopic examination did not seem to be indicated.

The clinical impression was squamous cell carcinoma of the upper lobe of the right lung with bony thorax and cervical sympathetic trunk extension. The tumor in the right supraclavicular region was removed surgically and showed a lymph node partially replaced by metastatic squamous cell carcinoma.

**COMMENT** Advanced squamous cell carcinoma of the right lung with extension to the ribs and cervical sympathetic trunk.

**Case 6**—M R, a 64-year-old white male, and a salesman by occupation until the onset of severe pain in the right chest in June, 1939. The pain was exaggerated by coughing and by deep inspiratory efforts. Deep heat therapy and numerous remedies had been used for the relief of the pain. The pain was severe in character and radiated from the back around to the upper part of the abdomen. In February, 1940, he developed hemoptysis which persisted until the time of admission to the hospital on May 5, 1940. He had had a cough which was different from the customary "cigarette cough" for a period of six months. He had lost 15 pounds in weight and was short of breath on moderate exertion.

*Physical Examination* The patient was an elderly white male, with acute pain in the right side of the chest. He described an area of tenderness and could easily point out its location in the midaxillary line. The examination was essentially negative with the exception of the chest findings. There was an area of localized tenderness over the sixth and seventh ribs in the midaxillary line, and pressure at this point reproduced the referred pain to the anterior abdominal wall. There was a respiratory lag on the right and the percussion note was altered in the region of the point of tenderness. The breath sounds were diminished over the lower lobe of the right lung. The routine laboratory studies were within the range of normal.

Roentgenologic examination revealed a 6 x 8 cm mass involving the lower lobe of the right lung and partial destruction of the sixth, seventh and eighth ribs. A bronchoscopic examination revealed no evidence of an intraluminary tumor.

On May 9, 1940, a biopsy of the chest wall and partially destroyed eighth rib revealed squamous cell carcinoma apparently of bronchogenic origin.

This patient was discharged from the hospital two weeks after his admission and advised to take morphine for the relief of his pain. He lived for a six-month additional period during which time he had severe and persistent pain in the right chest.

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*Autopsy* A squamous cell carcinoma of the lower lobe of the right lung was identified. Extensive destruction of the sixth, seventh, eighth and ninth ribs was present, however, there was no metastasis to the regional lymph nodes. A bronchopneumonia involved primarily the right upper lobe and lower lobe of the left lung.

*COMMENT* This extensive squamous cell bronchogenic carcinoma, associated with rib destruction, was operable and apparently curable at the time this patient presented himself for treatment. The author's experience in managing this type of patient suggested the likelihood of curability in such cases by a total pneumonectomy, with simultaneous block resection of the chest wall.

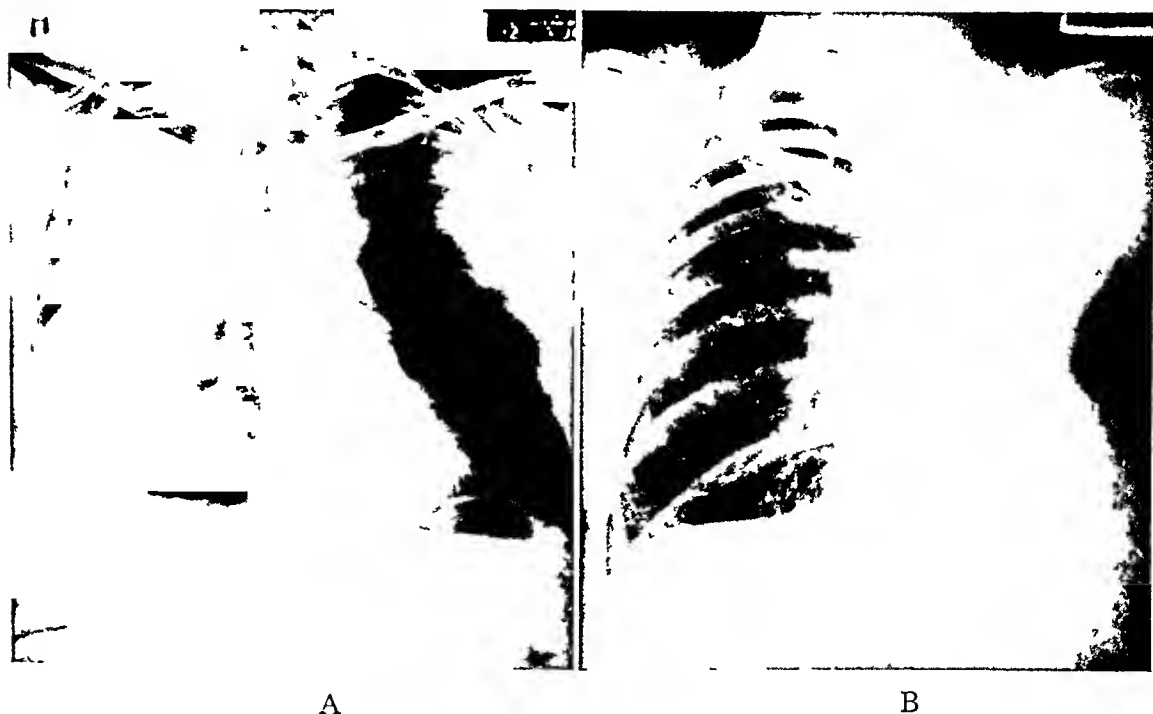


FIG 5—(A) Case 7 Regular PA roentgenogram of chest showing large peripheral squamous cell carcinoma of the lung, left  
(B) Case 7 Postoperative roentgenogram showing block excision of chest wall and total pneumonectomy, left

*Case 7—C L*, a 53-year-old white male, a farmer by occupation, developed pain in the left chest in January, 1946. The pain radiated from the precordial region posteriorly to the midportion of the back. Pain had been persistent in character and there had been frequent exacerbations of severe pain which required narcotics for symptomatic relief. Soon after the onset of pain in January, he began to have attacks of hemoptysis. Dyspnea had not been a troublesome symptom, except during the attacks of severe pain.

*Past History* He had had a chronic cough for 20 years, but there was no change in the cough until January, 1946. Six years prior to this hospital admission, he sustained a blow to the left chest which rendered him unconscious. Pain and soreness followed this injury, but he entirely recovered within a period of one month. He had pneumonia as a child which was complicated by a lung abscess. This healed without operative intervention. The family history is irrelevant.

*Physical Examination* The patient was in a good state of nutrition. The positive findings of the examination were limited essentially to the chest. There was a respiratory lag on the left. Percussion note was dull high in the axillary region and over the left scapular region. Breath sounds were diminished and vocal and tactile fremitus were

increased in these regions. Tenderness to palpation was present over the fourth, fifth, sixth and seventh ribs in the midaxillary line. The heart sounds were of good tone and quality. Blood pressure was 116/78. Kidney function tests revealed normal findings. Roentgenologic examination revealed a ten-centimeter mass in the lateral one-half of the left chest extending from a level of the third rib to a level of the seventh rib in the posterior axillary line (Fig 5). Overexposed films showed destruction of the fourth, fifth and sixth ribs in the posterior axillary line. *Clinical Diagnosis* Squamous cell carcinoma of the lung, with invasion of the ribs. Bronchoscopic examination was not carried out in view of the peripheral location of the tumor.

*Operation*—September 5, 1946. A total pneumonectomy on the left was performed, removing a block of the chest wall with the specimen. The second, third, fourth, fifth, sixth, seventh and eighth ribs were removed *en bloc*, dividing the ribs and neurovascular bundles posteriorly at their junctions with the transverse processes. The ribs and intercostal bundles were divided again at the anterior axillary line. This wide excision included the infiltrating tumor of the chest wall. During the operation 2,500 cc of citrated blood were given.

*Pathologic Report* Squamous cell carcinoma of the lung, with osseous invasion of the second, third, fourth, fifth, sixth and seventh ribs. The regional nodes showed no evidence of metastasis.

*Postoperative and Late Course* This patient's immediate postoperative course was complicated by his inability to cough and expel pulmonary secretions. Extensive decostalization of the chest wall was responsible for his inability to cough. This complication was managed by five postoperative bronchoscopic aspirations and repeated intratracheal catheter suction. Ten days postoperatively, he was able to be up and about, and the pulmonary secretions could be evacuated with ease.

**COMMENT** This was an advanced squamous cell carcinoma of the lung, with erosion of multiple ribs, apparently cured by radical surgery. Postoperative difficulty in evacuating secretions was again encountered in this patient.

#### SYMPTOMS AND DIAGNOSIS

Delay in diagnosis of this particular group of patients can be ascribed partially to the late manifestation of symptoms in carcinoma of the lung of peripheral origin. Pain preceded other symptoms, and it was of a severe character, persistent, and well-localized. Pain of months' duration often failed to direct attention to the possibility of a lung tumor. In the early stages pain may be present, but the roentgenographic appearance may easily be overlooked. Other than pain, there are few symptoms until late in the course of the disease. Tenderness to percussion and palpation was present in each case and the ribs or ribs invaded could be identified with ease.

Roentgenologic examination constitutes one of the best methods of diagnosis of either a peripheral or centrally-placed carcinoma of the lung. These cases reveal evidence of a peripheral, sharply circumscribed, and dense tumor mass. In the early stages the tumor mass is small and may be overlooked. Rib destruction is revealed by overexposing the films, and this examination frequently underestimates the extent of bony destruction. Intrapleural pneumothorax adds little additional information. Direct biopsy of the invaded rib will establish a tissue diagnosis, but it carries with it the danger of soft-tissue implantation in apparently operable patients. Needle biopsy has the objec-

tionable features of seeding cancer along the needle track, hemorrhage, and infection. Bronchoscopy is not indicated, for the tumors are peripheral in location. Exploratory thoracotomy is the method of choice in select cases for determining the tissue diagnosis and operability. The pleural cavity is entered a rib and full rib's interspace below the lesion. In addition to determining operability, this site of approach facilitates the technical procedure of block excision of the chest wall and lung. Involvement of the brachial plexus, sympathetic trunk, phrenic nerve and the transverse processes of the vertebrae contraindicate curative surgical attempts, but a palliative resection must be considered in view of the associated severe pain. If the postero-anterior roentgenologic view of the chest delineates lung tissue between the mesial border of the tumor mass and mediastinum, local operability has been established. Invasion of the serratus anterior muscle is not a contraindication to block excision, for such occurred in one patient (Case 2), who has survived for a period of six years.

#### TREATMENT AND RESULTS

The successful treatment of cancer of the lung invading the ribs depends upon extirpation of the local lesion and regional lymphatics. This embraces block excision of the chest wall leaving a margin of healthy tissue attached to the involved structures, total pneumonectomy, and resection of the regional lymph nodes. Although radical excision of the chest wall accompanying pneumonectomy will probably increase the mortality rate in general for cancer of the lung, it seems of little importance when the prognosis of these patients subjected to block excision and pneumonectomy is considered. The pathologic behavior of the type of cancer of the lung invading the ribs makes it suitable to block excision and a good prognosis will eventually be established by further experience. The postoperative management of these patients is more difficult in that decostalization of the involved hemithorax renders the cough ineffective. Repeated catheter suction and frequent bronchoscopic removal of the secretions has been necessary in my experience.

Five of the patients herein reported were subjected to block excision of the chest wall and pulmonary resection. A total pneumonectomy was carried out in four, and a palliative lobectomy in one. There was one operative death. The patient with a palliative lobectomy died 11 months postoperatively. The remaining three patients are living and well, one for six years, one for two years, and one for five months.

#### SUMMARY

Invasion of the ribs by primary carcinoma of the lung is not uncommon. The symptoms and methods of diagnosis have been discussed. The cell type and favorable pathologic behavior of these tumors makes them amenable to radical cancer surgery. Successful treatment embraces block resection of the chest wall, total pneumonectomy and removal of the regional lymph nodes. Five of the seven cases herein reported illustrate this method of treatment.

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# THE USE OF A MIXTURE OF PURE AMINO ACIDS IN SURGICAL NUTRITION\*

## I CERTAIN PHARMACOLOGIC CONSIDERATIONS

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### PART I

COX,<sup>1</sup> ELMAN,<sup>2</sup> AND OTHERS,<sup>3, 4, 5</sup> have shown that protein hydrolysates can replace protein for nutritional purposes. These materials have been extensively investigated clinically and certain practical difficulties in their use have become evident,<sup>6</sup> especially parenterally. The rate of intravenous administration is limited and the volumes required are large. To administer the equivalent of 90 Gm of protein requires eight or nine hours and a volume of 2,500 cc. This tires the patient, prevents ambulation or may interfere with sleep. Febrile reactions, nausea and vomiting may occur. The material may be irritating subcutaneously. There is, thus, still a need for protein substitutes that can be given parenterally without these limitations.

Recently, Madden<sup>7</sup> has studied various mixtures of pure amino acids in respect to their efficiency in regenerating plasma protein in the dog subjected to plasmapheresis. One of these mixtures, VUJ† was found to be useful for this purpose and was tried in a patient, a man with chronic ulcerative colitis. Nitrogen retention was shown by the patient, and so, presumably, protein formation. It, therefore, seemed desirable to give this material an extended clinical trial. The results of this study are presented in this and the subsequent papers.

### METHODS AND MATERIALS

First experiments were conducted with a 10 per cent solution of the amino acid mixture. Frequent spontaneous precipitation was noted upon refrigeration and made this solution unsafe for routine use. An 8 per cent concentration proved to be quite stable, providing a light, greenish-yellow, clear, bitter-tasting solution, which remained apparently unchanged for periods up to three months. This solution was given to most of the patients. A 5 per cent dextrose 8 per

\* The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Columbia University.

† 65 Gm of the VUJ mixture has the following composition:

dl-threonine	7.0 Gm	dl-tryptophane	1.2 Gm
dl-valine	9.0 Gm	dl-phenylalanine	4.5 Gm
l-leucine	10.0 Gm	dl-methionine	4.0 Gm
dl-isoleucine	7.0 Gm	l-histidine HCl	2.6 Gm
l-lysine HCl	8.0 Gm	l-arginine HCl	5.2 Gm
		glycine	6.5 Gm



cent amino acid mixture was tried on 12 patients but was not used further because of nausea, vomiting or mild temperature rise in 10 of the 12 cases

One liter of the 8 per cent amino acid solution provides about 9.6 Gm of nitrogen. About 14 per cent of the amino acids in solution is dextrorotatory and may be considered to be unavailable for protein anabolism. There is also a loss of 1 to 5 Gm of amino acid nitrogen by excretion as such into the urine, after the infusion of 1,500 to 3,000 cc.

The solution has a  $pH$  of 5.5. Because of this acidity, 480 cc of  $\frac{1}{6}$  molar sodium lactate solution were given to provide base when large amounts of the amino acids were used parenterally. A few trials were made intravenously of the amino acid solution after neutralization, but the material produced nausea or pyrexia after small amounts.

The 8 per cent material was employed in a total of 73 cases, some for periods up to three weeks and in amounts up to three liters per day. The usual method of administration was by infusion, and a total of about 350 infusions were given. The material has been given by hypodermoclysis in about 25 instances. Cardiac and renal function were evaluated before treatment and the fluids given through a venous pressure machine, when there was doubt. Varying rates of infusion of the amino acid mixture up to one liter per hour were tested. Blood  $CO_2$ ,<sup>8</sup> chlorides,<sup>9</sup> urea nitrogen,<sup>10</sup> and hematocrit<sup>11</sup> were followed by standard methods when treatment was continued for several days. The infusions generally were the sole source of nitrogen, with intravenous or subcutaneous supplements of 1,500 to 3,000 cc of a 5 per cent dextrose saline solution or occasionally of 480 cc of  $\frac{1}{6}$  molar sodium lactate solution. In other instances, food was given but the amino acid solution was provided to supplement an inadequate protein intake. Amino acid blood levels were occasionally determined after infusion.<sup>12</sup>

## RESULTS

*Reactions.* Nausea and vomiting were the only frequent ill effects of amino acid therapy. The occurrence of these symptoms appeared to be related to the rate and amount of administration. Amounts up to a liter per hour were given without reaction, but, in general, 400 cc per hour was the maximum speed consistently tolerated. Women may tolerate the material less well, though few trials were made in women. Data concerning the blood level of amino acid at the time of nausea is incomplete. Seventeen patients were studied. The blood amino N was elevated to between 9.6 and 25.8 mg per cent, 1.5 to 2.5 hours following the start of the infusion. One value of 32.5 mg per cent was observed. In general, nausea was found consistently with levels over 20 mg per cent (four cases). The blood level was restored to normal by several hours after infusion so that the division of the desired dosage into morning and afternoon infusions frequently avoided symptoms.

Hyperpyrexia and chills occurred in five patients. In three of these, the same amino acid solutions were readministered without recurrence of fever. Pyrogenic reactions<sup>13</sup> to glucose and saline were noted at this time throughout the hospital, so that these reactions probably resulted from faulty care of the

infusion sets In the other two cases, the amino acid mixture was administered during the course of a preexistent fever and was followed by a chill and temperature rise lasting for many days The reaction to the amino acid infusions may have been a coincidental flare-up of the original disorder, rather than a pyrogen response In any event, the incidence of febrile reactions is low \*

Thrombophlebitis was not noted as a result of the amino acid infusions except where a Lindemann needle was left *in situ* for several days after operation This maneuver produces venous thrombosis with dextrose or saline alone Venous spasm of the smaller veins of the lower arm and hand occurred relatively frequently with infusions into these sites, prolonging the infusion time considerably

Amino acids were given by hypodermoclysis in about 25 instances, 1,000 cc per day Cellulitis was noted once, although most of the patients began to complain of pain and tenderness during the treatment, especially after several clyses had been given

The carbon dioxide content of the blood was reduced by the administration of more than 2,000 cc per day of the amino acid solution and the fall was not prevented by the concurrent administration of 12 Gm of sodium chloride as a 5 per cent dextrose-saline solution or by the use of 480 cc of  $\frac{1}{6}$  molar sodium lactate solution The impression was gained, however, that sodium lactate may have lessened the degree of fall One death occurred associated with a drastic reduction in blood carbon dioxide content The complete history is given below

**Case Report**—P N, male, age 47, who underwent a partial gastrectomy and resection of a jejunal ulcer April 17, 1945

The history was essentially irrelevant except for some weight loss of about 10 or 15 pounds prior to operation Physical examination was negative Prior to operation a glucose tolerance test showed a fasting blood sugar of 142, at 5 hour 170, 1 hour 206, and 2 hours 143, although it was 52 at 3 hours On day 1 after operation, he received 1,500 cc 5 per cent glucose and saline, with 25 Gm sulfadiazine This was repeated on day 2 On day 1, a urea nitrogen was 21 mg per cent  $\text{CO}_2$  59.8 vols per cent Chloride 570 mg per cent On day 1, he received 1,500 cc 8 per cent amino acids On day 2, 3,000 cc On day 3, 1,500, and day 4, 1,500 On day 3, urea nitrogen was 40, with a  $\text{CO}_2$  of 20.2 and chlorides 662 This report was not received until after the amino acids was given on day 4 On day 5, he developed pulmonary edema, had a urine output of 190 cc, and a blood  $\text{CO}_2$  of 16 vols per cent, for which 40 Gm of sodium bicarbonate was given During the day his temperature rose to 104.8°F, and he died in 12 hours At this time his urea nitrogen had fallen to 23 mg per cent Aside from acidosis and pulmonary edema, the cause of death is unknown There was no autopsy

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\* The admixture of glucose, or the neutralization of the mixture with alkali, appears to alter the property and toxicity of the solution For this reason, dextrose-saline is not mixed with the amino acid solution, but precedes or follows it, or is given by a different route Also, such substances as sulfadiazine, vitamins for parenteral administration, or other intravenous medications, are not added to the amino acid solution but rather to the dextrose-saline The amino acid solution, like the hydrolysates, is an ideal medium for bacteria, so that any left-over solution must be discarded and not saved for later use, and the solution must not be allowed to stand open before use

Aside from this case, the lowest value for blood  $\text{CO}_2$  after 3,000 cc infusion a day for three days was 24 vols per cent, the average value about 40 vols per cent. Twenty patients were treated for three to five days with daily infusions of amino acid solutions. The range of values of lowest recorded blood  $\text{CO}_2$  levels was 16 to 57.9 vols per 100 ml of blood. The corresponding range in six controls was 53.2 to 73.0 vols per 100 ml.

The values for the highest blood urea nitrogen were 10 to 40 mg per cent in the treated patients and 13 to 26 mg per cent in the controls. The urea nitrogen values are no higher than is found after the ingestion of much protein, or with gastro-intestinal bleeding.<sup>14</sup>

*The Metabolism of Administered Amino Acids*—A rise in amino acid nitrogen in the urine was noted after infusion. Between 1 and 4 Gm of amino acid nitrogen per 24 hrs were lost in this form (Table I). The speed of

TABLE I

SHOWING EXTREME VALUES FOR AMINO ACID NITROGEN EXCRETION DURING FIRST WEEK AFTER OPERATION, AFTER 3 TO 5 DAYS TREATMENT WITH A MIXTURE OF PURE AMINO ACIDS

Patient	Amount of Infusion (cc)	Urine Amino Acid Nitrogen (Gm /24 Hr)
J C	2,000	2.42
J D	2,000	0.80
J H	2,000	4.16
W H	2,000	3.80
A K	1,000	1.72
C M	1,000	2.63
J N	2,000	3.0
W R	1,500-2,000	0.92
R S	2,000	3.02
E C	2,500	2.60
H J	2,500	2.34
A Z	2,500	1.90
E J	3,000	3.20
L J	3,000	2.38
P W	3,000	1.18
Control Cases		
F Y		0.56
M O R		0.57
A S		0.52

infusion had little effect on this value. The great bulk of the amino acid was converted into urea as evidenced by a rise of urea nitrogen in the blood and the greatly increased urinary nitrogen. The rest was utilized to form protein as evidenced by nitrogen balance and by the nitrogen sulphur ratio. This is discussed in a subsequent paper.

#### DISCUSSION AND CONCLUSIONS

A mixture of the ten essential amino acids and glycine has been subjected to a clinical trial and can be readily administered. About three quarters of the nitrogen is l-rotatory and is physiologically available as may be part of the d-rotatory material.<sup>15</sup> A rate of administration of 400 cc per hour appears to avoid any toxicity, at least in men, except in rare instances when nausea and

vomiting appear. Lowering of blood carbon dioxide content and rise in urea nitrogen occur with more than 2,000 cc of the 8 per cent solution a day. The rise in urea nitrogen is no more than occurs with similar amounts of beef protein.<sup>14</sup> There is no evidence of renal damage<sup>16</sup> either in the urine or in delayed return of blood values to normal with stopping treatment.

An infusion of 1,500 cc of this solution provides the average daily requirement of 15 Gm of available nitrogen, about 95 Gm of protein equivalent, and can be given in about four hours. About 350 calories are furnished, since most of the dextro-rotatory, and presumably physiologically inactive, isomers are also burned. Caloric supplements must be given along with the amino acids, as food or as dextrose-saline solution. Fifteen hundred cubic centimeters of 5 per cent dextrose-saline solution provide 75 Gm of sugar or 300 calories. Thus, 1,500 cc of amino acid solution must be supplemented by a minimum of 3,000 cc of 5 per cent dextrose-saline solution or dextrose in water, to give the patient a total of 950 calories, not counting the 1 to 4 Gm of amino acid nitrogen which are excreted unchanged in the urine and so are lost for combustion purposes—about 80 calories.

It is feasible to give as much as 1,500 cc of the amino acid solution twice daily to provide 28.8 Gm of nitrogen, the amount of supplementary 5 per cent dextrose-saline is reduced to 1,500 cc so as not to overload the circulation. Thus, a total of approximately 1,000 calories and the equivalent of about 180 Gm of protein is given in 4,500 cc. The only apparent danger with the larger doses is the progressive fall in blood carbon dioxide content after several days of therapy and the rise in blood urea nitrogen. Emaciated patients who cannot afford to lose from their fat stores can only be treated for short periods by this technic to build up their body protein stores, unless some calories are taken by mouth. However, the still relatively well-nourished hypoproteinemic patient can build up protein in this way, at the expense of fat, for long periods, if the amino acids are used to supplement an inadequate food intake.

Again, mention should be made of the importance of the evaluation of cardiac reserve prior to therapy and of observation of the patient with limited reserve during infusion by means of vital capacity and venous pressure. It might be mentioned that at a rate of 400 cc per hour even patients known to be on the border of failure have tolerated large amounts of amino acid without difficulty. In these patients the glucose supplement is given by clysis so that it will not be readily absorbed should signs of cardiac failure supervene. It should also be mentioned that amino acids should not be used when there is any indication of renal damage, in view of the acidosis and the rapidity of urea nitrogen accumulation in the blood which results even with normal kidney function. The one death in this series, however, cannot be explained by renal failure. Acidosis may have been responsible for the fatal outcome. Evidence of hypersensitivity was not noted although it is improbable that such reactions would occur with pure amino acids. Thus, the cause of death is obscure but may be related to the deaths reported with casein hydrolysates.

The above discussion has been chiefly limited to parenteral therapy. The availability of a compound which can replace or supplement dietary protein

intake by vein does not alter the fact that food is the best approach to adequate nutrition and should be given whenever possible. The protein in food is more efficiently utilized over long periods and provides at least some minerals and vitamins, as well as higher calories. However, if necessary, the amino acids provide an ideal supplement for an inadequate food intake and are most simply and efficiently used in this way.

As yet the use of the VUJ mixture of amino acids is limited by the high cost. A nontoxic hydrolysate of approximately the same composition would be equally suitable for nutritional purposes. However, if no such product becomes available, it is possible that an increased demand for this material will enable production costs to be reduced considerably.<sup>1</sup>

### SUMMARY

1 A mixture of pure amino acids in 8 per cent solution has been given an extensive clinical trial, parenterally.

2 Few toxic effects have been noted with the 8 per cent solution. The incidence of nausea and vomiting, reduction in blood carbon dioxide content and urea nitrogen, and the excretion of unchanged amino acids is recorded.

3 The case report of one death of obscure origin, possibly from acidosis, is presented.

4 The available nitrogen and calories that can be given as pure amino acids is discussed and the use as a sole source of nitrogen or as a supplement to food is discussed.

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## PART II

### EFFECTS UPON NITROGEN BALANCE

IT IS WELL-ESTABLISHED that one of the results of injury to the body is the appearance of negative nitrogen balance on the same nitrogen intake which previously maintained equilibrium<sup>1-5</sup> It is disputed as to whether an increase in the nitrogen intake will reestablish equilibrium or whether new mechanisms make this impossible Investigation of this problem is hindered by the poor appetite of the patients so that high nitrogen intakes are generally difficult to achieve Recently, a mixture of pure amino acids<sup>6</sup> has become available and it has been possible to give reasonably large amounts of nitrogen parenterally with somewhat less difficulty than with protein hydrolysates<sup>7\*</sup> The results of this experience are presented here as is a concept of the mechanism responsible for the negative nitrogen balance after injury, suggested by these data

### METHODS

A metabolism ward set-up was established on one of the surgical floors of the Presbyterian Hospital Special nursing and orderly care, a dietitian and diet kitchen for the project were provided Urine, stools, gastric drainage and vomitus were collected in 24-hour amounts and analyzed daily for nitrogen<sup>8</sup> Urines were preserved with chloroform in the ice chest, the other specimens under concentrated sulphuric acid Urine creatine, creatinine and total neutral 17-ketosteroid determinations were done early in the study but were abandoned

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\* Dr D F Robertson, of Merck and Co , generously supplied the solution of pure amino acids (VUJ) which made this study possible

after it was established that correlation with the effects of operation was not significant. Urine total sulphate<sup>9</sup> and amino acid nitrogen excretion<sup>10</sup> were followed daily in most cases. Amino acid intake was determined by weighing the containers before and after administration. Food nitrogen intake was estimated by standard tables, with occasional check nitrogen determinations on samples of the diet. A casein hydrolysate† was used in some instances as a supplementary source of nitrogen and sugar. Most patients received a single transfusion of 500 cc of blood after operation. This protein does not appear in the urine for a number of days<sup>11</sup> after transfusion, so the nitrogen involved was not entered into the balance calculations. Because of the transfusion and fluids given during operation, amino acid infusions were not begun until the day after operation, to avoid overloading the circulation. In the early work, amino acids were given throughout the day for each of the first three days. This was changed later to a program in which up to 1,500 cc of the 8 per cent amino acid solution were given both morning and evening by infusion, supplemented by a clysis of 1,500 cc of 5 per cent dextrose in saline, in the morning. The patients received water by mouth for the first two to three days after operation. A standard postoperative gastric feeding regimen was then started. Food intake was increased as rapidly as tolerated. As the calories increased by mouth, the dextrose in saline was omitted. As the protein intake became greater, the amount of the amino acid infusion was reduced. Thus, most patients received amino acids in decreasing quantities for about six days after operation. Determinations of venous pressure and vital capacity<sup>12</sup> were made when there was doubt as to cardiac function. Blood urea nitrogen, carbon dioxide content, chlorides, hematocrit, red blood cell count, and plasma proteins were determined by standard methods,<sup>13-17</sup> the blood chemistry estimations being done two or three times a week postoperatively.

## RESULTS

*Healthy Subjects* A preliminary short-term experiment was conducted to confirm the adequacy of the VUJ mixture of pure amino acids as a substitute for protein in the diet. Two young healthy men, working as orderlies in the hospital, were placed on a weighed diet with 90 Gm of protein per day and 3,000 calories. When nitrogen equilibrium was established for a week, 1,000 cc of 8 per cent amino acid solution by infusion were substituted for 60 of the 90 Gm of protein in the diet. Some food protein was given in order not to alter the ratio of protein, fat and carbohydrate on which nitrogen equilibrium had been produced. The substitution of amino acid for the food protein produced no significant change in nitrogen balance during the two days of its use or in the next few days.

*Preoperative Patients* The mixture of pure amino acids was given to 15 patients before operation. In six of the patients, the amino acid solution was

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† Dr Warren Cox and Mr A Hill, of the Mead Johnson Co, kindly supplied the casein hydrolysate (Amigen) for oral and parenteral use.

# AMINO ACIDS IN SURGICAL NUTRITION

TABLE II  
SHOWING PREOPERATIVE NITROGEN BALANCE WITH A MIXTURE OF PURE AMINO ACID  
AS A SUPPLEMENT TO FOOD OR CASEIN HYDROLYSATE

Patient	Day Before Oper	Food Nitrogen (Gm )	Casein Hydrolysate Nitrogen (Gm )	Amino Acid Nitrogen (Gm )	Total Nitrogen Intake (Gm )	Total N Excretion Urine and Stool (Gm )	Nitrogen Balance (Gm )
J B	9	13 1			13 1	14 4	- 1 3
	8	15 8			15 8	13 7	+ 2 1
	7	15 8			15 8	14 6	+ 1 2
	6	16 6			16 6	10 7	+ 5 9
	5	18 0			18 0	12 9	+ 5 1
	4	17 0		9 5	26 5	19 4	+ 7 1
	3	16 9		9 6	26 5	18 5	+ 8 0
	2	18 6		9 6	28 2	13 4	+14 8
	1	10 4			10 4	19 8	- 9 4
G McG	4	1 1		26 9	28 0	24 1	+ 2 8
	3	0 9		28 9	29 8	26 8	+ 3 0
	2	0 4		28 8	29 2	28 7	+ 0 5
	1	0 3		12 3	12 6	14 0	- 1 4
S K	6			18 5	18 5	9 2	+ 9 3
	5		18 0	19 0	37 0	16 9	+20 1
	4		18 0	19 0	37 0	16 8	+20 2
	3		17 4	17 6	35 0	18 2	+16 8
	2		18 0	14 7	32 7	13 5	+18 2
	1			9 8	9 8	12 9	- 3 1
	0			12 2	12 2	15 9	- 3 7
M F	7	0 2	13 0	9 7	22 9	22 3	+ 0 6
	6	1 3			1 3	11 8	-10 5
	5	7 4	10 2	9 1	26 7	14 6	+12 1
	4	4 1	13 0	9 5	26 6	21 3	+ 5 3
	3	6 1			6 1	10 4	- 4 3
	2	10 6			10 6	6 8	+ 3 8
	1	11 1			11 1	5 8	+ 5 3
R G	14		19 8		19 8	22 0	- 2 2
	13		19 4		19 4	22 0	- 2 6
	12			14 0	14 0	15 8	- 1 8
	11			14 1	14 1	26 3	-12 2
	10			13 6	13 6	13 6	0 0
	9			9 7	9 7	20 6	-10 9
	8		13 2		13 2	16 2	- 3 0
	7		13 2		13 2	12 0	+ 1 2
	6				0 0	10 2	-10 2
	5		20 0		20 0	9 6	+10 4
	4		22 2		22 2	14 5	+ 7 7
	3	7 3			7 3	10 8	- 3 5
	2	29 4			29 4	9 9	+19 5
	1	30 5			30 5	15 5	+15 0
	0			14 0	14 0	12 8	+ 1 2
R S	7	0 1	19 2		19 3	10 2	+ 9 1
	6	0 8		13 9	14 7	3 3	+11 4
	5		6 6	14 3	20 9	17 9	+ 3 0
	4		12 8		12 8	26 9	-14 1
	3		12 8		12 8	14 9	- 2 1
	2			13 8	13 8	19 6	- 5 8
	1			13 4	13 4	16 9	- 3 5
	0			9 5	9 5	20 2	-10 7



given in addition to nitrogen taken in the diet or taken in a casein hydrolysate material (Table II) Nitrogen was retained when the nitrogen intake was high, whether the amino acids were given alone or as a supplement However, smaller intakes of about 10 to 14 Gm nitrogen, sufficient to maintain equilibrium when given as food, were not adequate when administered as pure amino acids, or as casein hydrolysate without food Also, negative balance occurred and persisted for several days after changing from high to low nitrogen intakes This is seen with changes in food nitrogen intake and is not peculiar to the parenterally given materials

The small supplies of material in the early phase of the study limited efforts to study the adequacy of amino acid administration and glucose as the sole source of nutrition preoperatively, although this was accomplished post-operatively More data are being accumulated

*Postoperative Patients* A total of 29 patients were given the mixture of pure amino acids as the only source of nitrogen for the first three to five days after operation Calories were supplemented by glucose-saline solution Twenty-one of the patients underwent partial gastrectomy for peptic ulcer, while the other patients had a variety of operative procedures An additional six gastrectomy patients were followed as controls, in that they were treated exactly the same as the other gastric cases but were given no amino acids

#### A NITROGEN BALANCE AFTER PARTIAL GASTRECTOMY

The least amount of nitrogen lost by any of the six control patients subjected to partial gastrectomy and given no amino acids postoperatively, was 25 Gm of nitrogen, in the first five days after the procedure Seventeen of the 21 patients undergoing the same procedure (Table III, Charts 5 and 6) but treated with amino acids, lost varying amounts less than this (Table III,

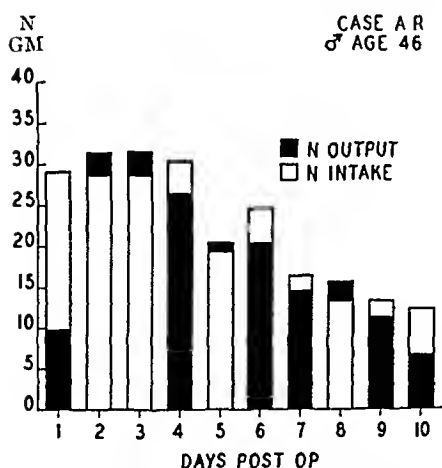


CHART 1—Showing the production of nitrogen equilibrium after partial gastrectomy, by the use of a mixture of pure amino acids

Charts 1-3) Three of these 17 patients remained in nitrogen balance for this period and six showed actual positive balance There was considerable wastage of amino acid material, as shown by a high urinary nitrogen excretion Some of the wastage may have been the result of the low calories supplied, so that part of the amino acids were diverted for fuel

One peculiarity in the transition from amino acid to food intake was noted in three patients When amino acid administration was stopped before an equivalent intake was achieved in the diet, the excretion of urinary nitrogen continued at a high level (Chart 4) This produced a consequent sharp negative balance which

was sufficient, in a day or two, to exceed the total negative balance of the controls for the entire first five days after operation This was prevented

AMINO ACIDS IN SURGICAL NUTRITION

TABLE III  
SHOWING POSTOPERATIVE NITROGEN BALANCE FIGURES,  
AFTER PARTIAL GASTRECTOMY

N Balance Gm First 5 Days	Amino Acid Treated		Controls
	Adequate	Inadequate	
> +10	4	1*	0
0 +10	1	0	0
-1 -10	5	2	0
-11 -20	3	1	0
-21 -30	2	1	4
-31 -40	1	0	1
-41 -50	0	0	1

(\* Renal damage)

by reducing the amino acid input only as food intake was increased to the same degree

(1) *Effect of Weight Loss Upon Nitrogen*—Inanition and debility abolish the tendency toward negative nitrogen balance which usually occurs after injury. The weight loss of the patients was thus examined to determine if this was a factor in the retention of nitrogen. Seven treated cases with little or

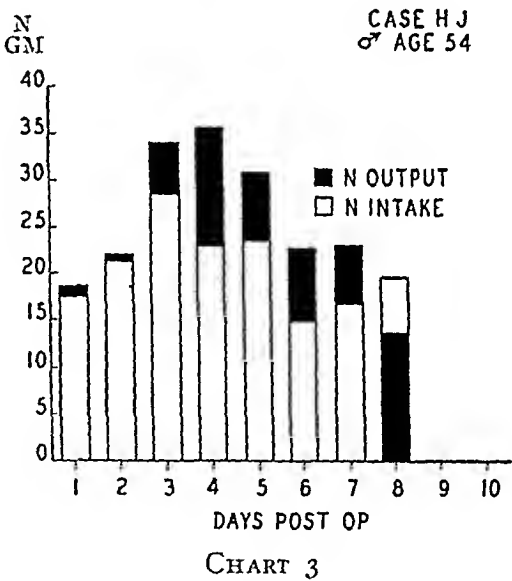
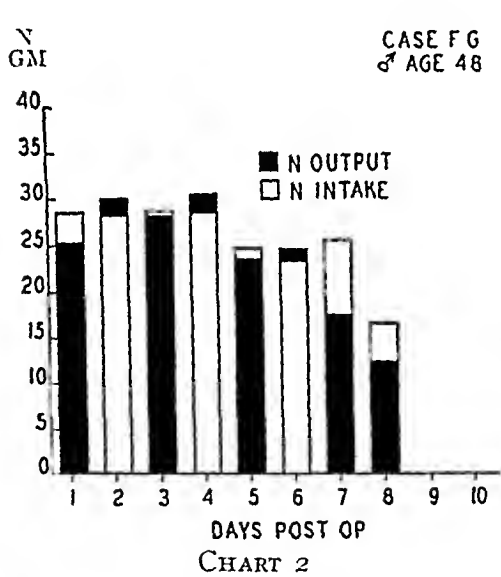


CHART 2—Showing marked nitrogen sparing after partial gastrectomy, by the use of a mixture of pure amino acids  
CHART 3—Showing the failure to spare nitrogen after partial gastrectomy with the use of a mixture of pure amino acids

no nitrogen loss after operation and four treated cases with maximum nitrogen loss showed a difference (Table IV) in preceding weight loss. Two in each group had lost no weight but four had lost 25 to 30 pounds in the group retaining nitrogen, whereas, the greatest weight loss in the group not retaining nitrogen was 10–19 lbs in two cases. Thus, although weight loss was not a reliable index of debility or of the ease with which nitrogen balance was going to be established, there was a tendency in the gastric cases to retain nitrogen more readily if the previous weight loss was marked.

(2) *Effect of Level of Amino Acid Administration*—The data have been examined to determine if the level of nitrogen intake is important in the pro-

duction of nitrogen balance A consideration of the amount of nitrogen administered to that retained indicates a relationship Low nitrogen intakes of 0.11 to 0.30 Gm N/Kg body weight, were generally associated with negative balance and higher intakes with nitrogen sparing, if not balance There is considerable variability Unlike the situation before operation, no critical level of nitrogen intake was established beyond which nitrogen balance was uniformly produced, but no greater intake than 0.50 Gm N/Kg body weight was achieved

TABLE IV

SHOWING RELATION OF WEIGHT LOSS BEFORE OPERATION TO NITROGEN BALANCE AFTER OPERATION  
PARTIAL GASTRECTOMY TREATED WITH A MIXTURE OF PURE AMINO ACIDS

Preoper Weight Loss % Average Body Weight	Nitrogen Balance					
	> +10 (Gm N)	+10 to 0 (Gm N)	-1 to -10 (Gm N)	-11 to -20 (Gm N)	-21 to -30 (Gm N)	-31 to -40 (Gm N)
0	1	0	1	1	2	
1-10	1	0	3	2	1	1
11-20	3	1	2	1	0	0
21-30	0	0	1	0	0	0

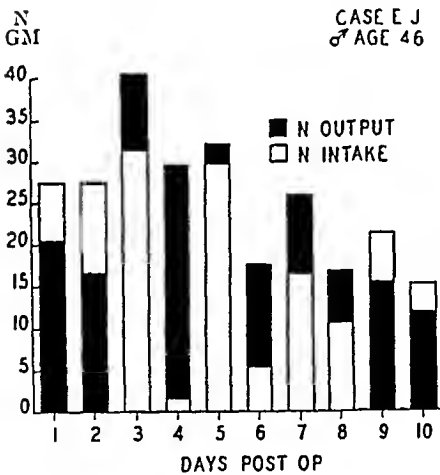


CHART 4

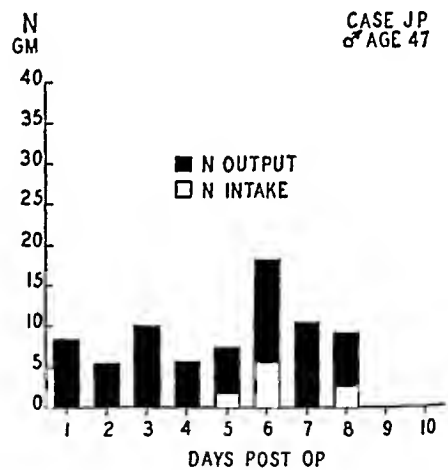


CHART 5

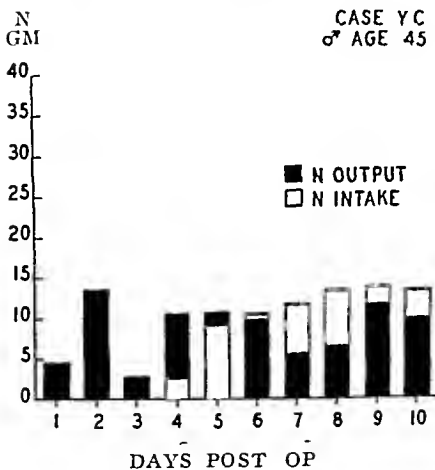


CHART 6

CHART 4—Showing the continued outpouring of nitrogen after the sudden cessation of a high nitrogen intake, and the nitrogen sparing effect of resumption of high nitrogen administration

CHARTS 5 and 6—Showing nitrogen loss after partial gastrectomy on the usual postoperative regimen without amino acid administration

(3) *Total Sulphate Excretion*—The total sulphate excretion in the urine was determined to see whether retained nitrogen was used for protein synthesis. Sulphate excretion tended to parallel nitrogen output (Chart 7). The sulphur-nitrogen ratio averaged about 1:15. Thus, the variations in nitrogen balance probably involved tissue protein sources.

#### B NITROGEN BALANCE IN CASES OTHER THAN GASTRECTOMY

Eight operative patients, other than the gastrectomy cases, were given as high nitrogen regimens, as possible by parenteral route, immediately after operation and the effect of nitrogen balance observed. This group had, in general, been healthy prior to operation and had lost no weight, except the two pancreaticoduodenectomy patients. All received the VUJ mixture of pure amino acids until the food intake provided about 15 Gm of nitrogen per day. A casein hydrolysate was occasionally used to supplement the amino acid mixture when the supply of the latter had run out. In addition, two fracture patients were studied, a man and a woman in good health prior to the accident. The fractures were severe,

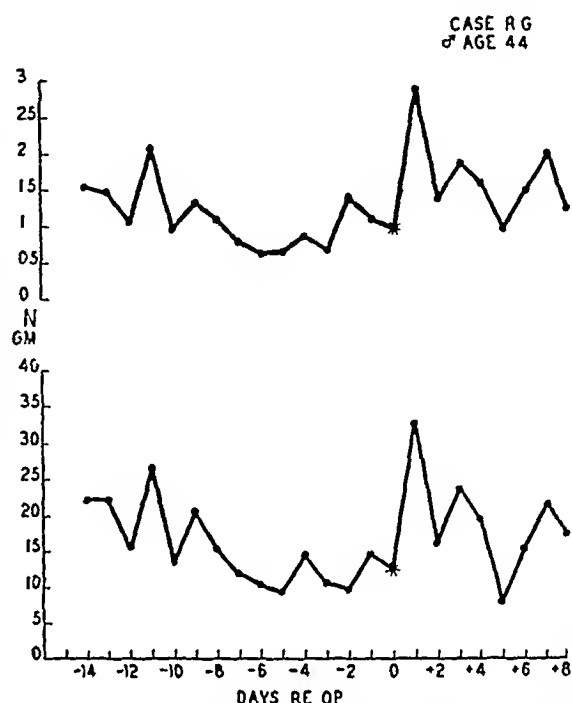


CHART 7—Showing the parallel excretion of total nitrogen and total sulphur before and after partial gastrectomy and amino acid administration.

TABLE V

SHOWING EFFECT OF TREATMENT WITH A MIXTURE OF PURE AMINO ACIDS UPON NITROGEN BALANCE AFTER MISCELLANEOUS OPERATIONS UPON PREVIOUSLY HEALTHY PATIENTS

Diagnosis	Patient	Treated Cases				Untreated Cases		
		Days of Rx	Total Intake (Gm N)	Total Output (Gm N)	Daily Balance (Gm N)	Days	Daily Balance (Gm N)	Source
Acute appendicitis with appendicectomy	D C	5	120.7	120.8	-0.0	4	-3.3	Grossman et al. <sup>11</sup>
	L J	3	64.9	69.5	-1.5	7	-3.6	
	J C	3	76.0	95.7	-6.6	3	-10.3	
	C M	4	95.6	107.4	-3.9	7	-3.3	
Hernia repair	C Q	4	71.4	75.2	-0.9	5	-0.2	Grossman et al. <sup>11</sup>
	A E	4	89.0	80.1	+2.1	6	-3.3	
Pancreto-duodenectomy	L C	5	94.7	123.4	-5.7	10	-2.4	Brunschwig et al. <sup>17</sup>
	A K	5	90.2	108.4	-3.6	10	-6.1	
Perforated ulcer	E McK	5	85.9	131.4	-9.1	10	-13.6	Brunschwig et al. <sup>11</sup>
Fracture	B McN	22	835.5	788.4	+2.1	39	-4.9	Howard et al. <sup>23</sup>

one of the lower third of the femur with much soft-part damage, treated by a plaster encasement after closed reduction, and the other both bones of the leg with open reduction. The man was placed on a diet of 60 cc of a 30 per cent solution of casein hydrolysate and 100 to 120 cc of high protein milk every hour for eight to 12 hours, and the woman on a fixed diet with 90 Gm protein and 2,500 calories supplemented with casein hydrolysate.

Nitrogen loss was decreased in half of the operative patients of this group, as compared to control figures in the literature for nitrogen loss after corresponding procedures (Table V). A discussion of the failures follows later in the paper. The fracture patients were maintained in nitrogen equilibrium after the trauma (Table VI), as opposed to the experience of Cuthbertson and

TABLE VI

TABLE SHOWING THE MAINTENANCE OF NITROGEN BALANCE IN A PREVIOUSLY HEALTHY MAN AFTER FRACTURE OF THE LOWER FEMUR WITH CONSIDERABLE SOFT PART DAMAGE (TREATMENT WITH PLASTER ENCASEMENT). THE EARLY FAILURE OF PLASMA PROTEIN AND HEMATOCRIT TO BE MAINTAINED IS ILLUSTRATED.

Case	B McN	Male	Age 66	N Intake (Gm)				N Output (Gm)				Nitrogen Balance (Gm)	Plasma Protein (Gm %)	Hema- tocrit (%)
Day Post Injury	Food	Casein Hydro- lysate	Total	Urine	Stool	Vomit	Total							
3	8.5	14.7	23.2	32.5			32.5				- 9.3			
4	12.5	21.9	34.4	27.4	0.4	0.3	28.1				+ 7.0	6.4	36.9	
5	14.5	23.1	37.6	34.3	0.4		34.7				+ 2.9			
6	14.9	23.2	38.1	21.5	1.7		23.2				+14.9	5.5	29.8	
7	14.5	21.2	35.7	26.8	2.1		28.9				+ 6.9			
8	20.2	23.3	43.5	41.9	2.1		46.1				- 0.5			
9	18.8	23.2	42.0	36.0	0.9		36.9				+ 5.1	6.3	33.0	
10	23.8	26.9	50.7	41.3	0.9		42.2				+ 8.5	6.5	34.8	
11	23.9	28.7	52.6	40.7	1.7		42.4				+10.2	7.0	38.0	
12	23.9	29.2	53.1	49.8	1.7		51.5				+ 1.6	6.9	37.0	
13	22.0	29.5	51.5	49.0	5.4		54.4				- 2.9	6.8	35.5	
14	23.8	28.6	52.4	46.6	1.8		48.4				+ 4.0	6.5	35.8	
15	23.9	29.3	50.2	45.9	1.8		47.7				+ 2.5			
16	20.2	23.2	43.4	47.4	1.7	0.1	49.2				- 5.8	6.8	37.2	
17	19.7	23.4	43.1	39.9	3.7	0.8	44.4				- 1.3	6.1	38.1	
18	19.5	23.4	42.9	43.1	2.8		45.9				- 3.0	7.5	42.3	
19	15.8	11.2	27.0	24.5	1.9		26.4				+ 0.6	6.9	42.2	
20	18.5	11.9	30.4	30.2	1.9		32.1				- 1.7	7.3	43.7	
21	15.9		15.9	21.5	1.8		23.3				- 7.4	7.4	43.7	
22	18.0		18.0	16.3	1.9		18.2				- 0.2			
23	18.3		18.3	14.8	1.8		16.6				+ 1.7			
24	15.7		15.7	15.4	1.8		17.2				- 1.5			

of Howard. A discrepancy was noted between nitrogen balance, plasma protein and red cell count in that the latter values fell during the first two weeks after the fracture despite the maintenance of nitrogen balance.

#### DISCUSSION AND CONCLUSIONS

The healthy adult remains in nitrogen equilibrium except for minor daily fluctuations. Slight changes in nitrogen intake result in a corresponding retention or loss of nitrogen from tissue reserves.<sup>18, 19</sup> This implies a balance between nitrogen synthesis and breakdown provided the minimal glucose and caloric

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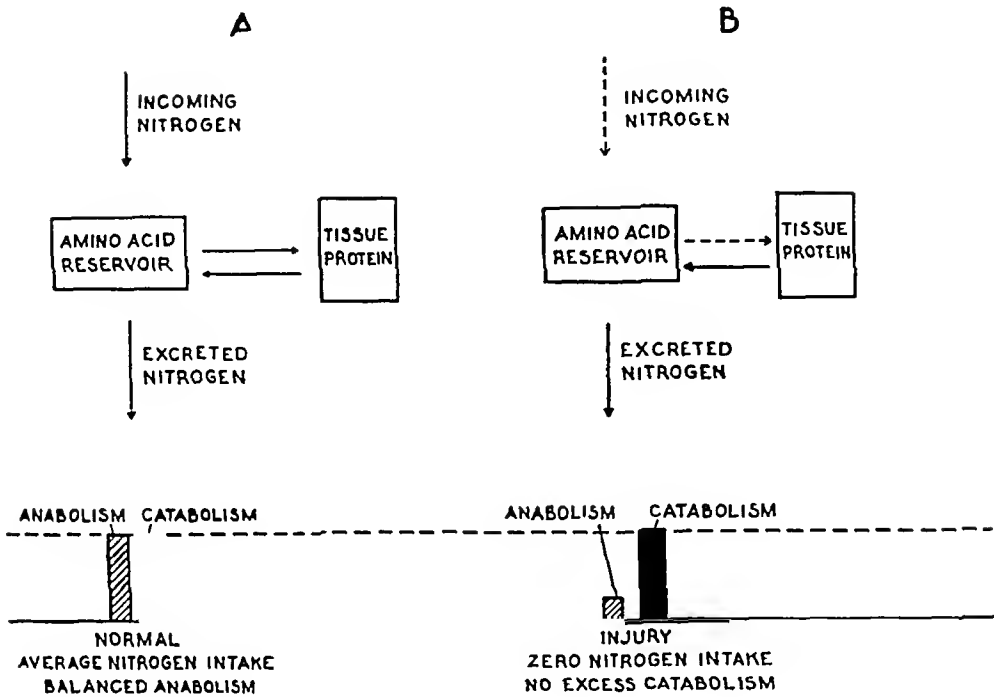


CHART 8

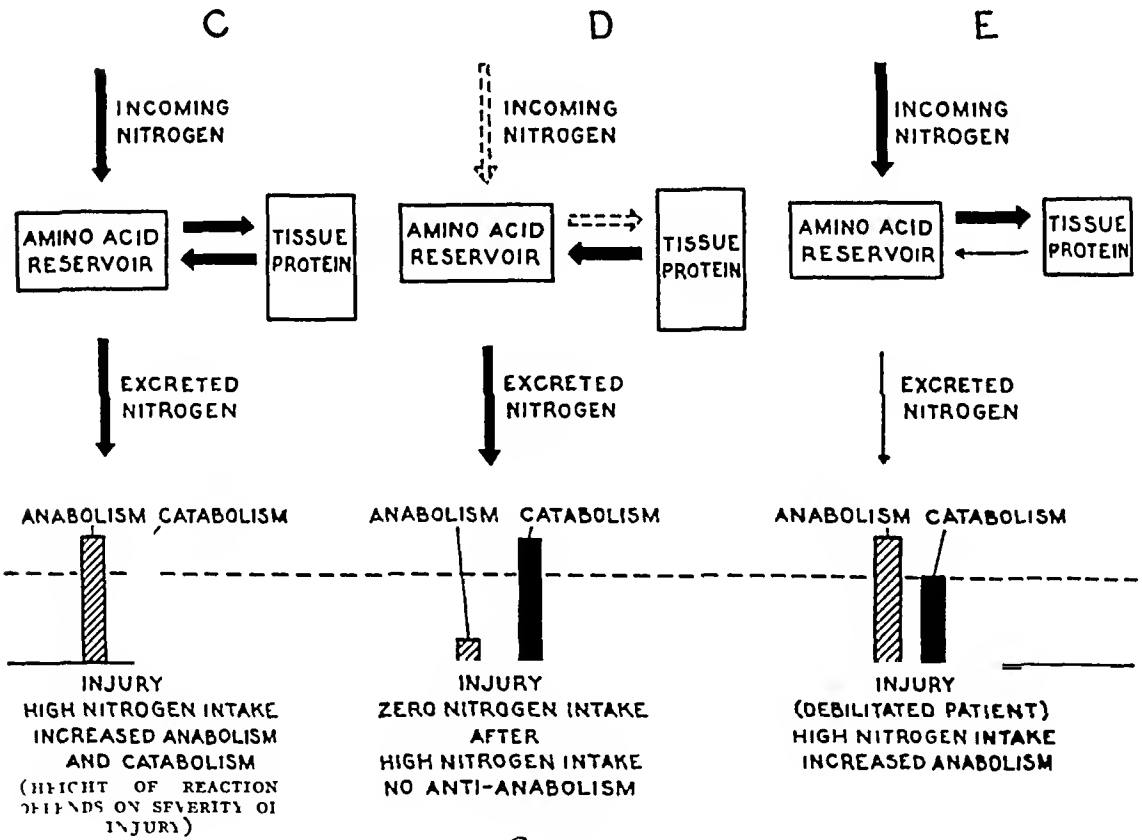


CHART 9

CHARTS 8 and 9—Presenting a schematic representation of the changes in nitrogen balance which occur after injury (Form of diagram suggested by Albright <sup>21</sup>)

requirements have been met (Chart 8a) Incidentally, this equilibrium point is somewhat higher in the men in this series,<sup>20</sup> 15 Gm of nitrogen intake per day (95 Gm protein) than the commonly accepted one of 10 Gm (60 Gm protein)

After injury, there is an acute change and a negative balance occurs when the nitrogen intake is maintained at previous levels This loss of nitrogen has been called the toxic destruction of protein and has been discussed since before 1894<sup>3</sup> Cuthbertson<sup>21, 22</sup> revived the concept that injury was followed by a phase of catabolism, since he could not restore his patients to nitrogen balance even with moderate increases in nitrogen intake He has been supported in this view by Howard, and others<sup>23, 24</sup> However, a catabolic response implies that stopping nitrogen intake from the time of injury would, if anything, increase the loss of nitrogen from the body The data of the present study show that this is not the case (Chart 8b) No excesses of nitrogen appear in the urine when nitrogen is withheld postoperatively and, in fact, the nitrogen excretion may be less than that of an uninjured patient on the same intake Also, high carbohydrate regimens spare nitrogen<sup>1</sup> which is unlikely if the nitrogen loss is the result of a true toxic destruction of tissues Thus, there is no increased rate of catabolism or tissue destruction in the absence of nitrogen intake, and the "catabolic phase" of injury is not an accurate description

A different theory to explain the inability to spare nitrogen has been advanced, namely, that incoming nitrogen is routed through the liver after trauma and is wasted before it can be used for anabolism by the tissues Thus, the loss of nitrogen is "antianabolic" rather than "catabolic"<sup>25</sup> However, the data of the present study indicate that incoming nitrogen is not entirely wasted, so that a high nitrogen intake lessens or reverses negative nitrogen balance after trauma (Chart 9c) This is evident when the nitrogen lost by the treated patients is compared with that of the untreated controls in the gastrectomy group, or with the figures in the literature for loss after the other procedures and especially fracture CoTui, *et al*,<sup>26</sup> Brunschwig, *et al*,<sup>27</sup> Levenson, *et al*,<sup>28</sup> and others, have presented data similar to those of the present study Thus, it is clear that the mechanisms for nitrogen retention or anabolism remain operative after injury so that an "antianabolic" explanation of events is dubious Further evidence against a solely antianabolic effect is seen when a high nitrogen intake after operation is suddenly stopped Nitrogen continues to be poured into the urine and must come from the tissues (Chart 9d)

Thus, the behavior of the nitrogen balance after injury is not satisfactorily explained by either the catabolic or antianabolic theories The simple assumption that there is an increase in the rate of both anabolism and catabolism, rather than a change in either, appears to solve the discrepancies It explains the fact that an increased nitrogen intake can reestablish nitrogen equilibrium and that more or less than this amount results in varying degrees of positive or negative nitrogen balance as in the healthy subject It also explains the continued outpouring of nitrogen from the tissues when the high nitrogen

intake is suddenly stopped. The fact that this evidence of increased catabolism is not present if nitrogen has not been given after the trauma, indicates one necessary condition in addition to the injury, for the response to be elicited, namely, the presence of incoming nitrogen. Another condition is that there have not been recent preceding injuries or body wasting from inanition. Madden<sup>29</sup> has suggested that reserve protein stores<sup>18</sup> are necessary for the reaction to trauma to occur. It is also possible that the mechanisms for catabolism, under these conditions, become too inactive to be easily activated by a new insult, so that nitrogen sparing continues to predominate (Chart 9c). A third factor is the severity of the injury, in that the more severe the insult, the more nitrogen is needed to restore equilibrium, *e g*, fractures versus partial gastrectomy.

In this connection, the use of gastric patients to study postoperative nitrogen balance lends itself to the just criticism of Peters<sup>30</sup> that such patients may be debilitated and may not be able to respond with a vigorous trend towards negative balance. Such a tendency is shown by the gastric cases of this series. However, three gastric cases put into nitrogen equilibrium had lost insignificant amounts of weight, and so were presumably otherwise healthy as were the fracture cases and the miscellaneous cases which were spared nitrogen. Also, the variations in amounts of nitrogen retained in the gastric cases after a given intake of nitrogen suggests that the usual reaction to trauma is operative. It is, therefore, felt that the nitrogen sparing from therapy is not entirely the result of debilitation and that the results are in line with those of Brunschwig, and the other workers, previously mentioned.

The significance of the fact that some patients were not restored to nitrogen balance, or spared nitrogen, deserves discussion. It is possible that these cases represent instances of a pure catabolic or antianabolic response to trauma. It is equally possible that insufficient nitrogen was given. With the pure amino acid mixture, the volume of fluid required and tendency to acidosis makes it practically impossible to administer more than 28 Gm of nitrogen a day. Thus, the nitrogen needs after a particularly vigorous reaction to trauma, such as with the two fracture cases, could not be met by parenteral feeding, and a negative nitrogen balance would occur. It is generally agreed that the intensity of the reaction to injury depends on the severity of the injury and the reactivity of the patient. Thus, it is felt that the cases with negative nitrogen balance, despite amino acid administration, represent a particularly vigorous response to injury wherein the nitrogen needs exceeded the amount of nitrogen administered. This is the reason for the failure of most investigators to overcome the tendency to negative nitrogen balance—not enough nitrogen was given.

It should be mentioned that the attainment of nitrogen balance does not mean that individual protein functions may not still be disturbed. Although the parallel retention of sulphur and nitrogen suggests that protein is being formed when nitrogen loss is diminished, as shown by the fracture patient, plasma protein and hematocrit may fall notwithstanding this. Thus, some tissues apparently build protein while others do not, and such a derangement may not be



reflected by the over-all nitrogen balance. The change is possibly too great to be explained by the factor of hemodilution.

Finally, it is of interest to determine whether the effects of nitrogen administration upon nitrogen balance are reflected on the clinical course of the patients. This is discussed in the next paper (PART III) of this series.

#### SUMMARY

1 A study has been made of the effect of a mixture of pure amino acids on nitrogen balance as a supplement to food or a casein hydrolysate preoperatively, and as the sole source of nitrogen for the first 3-5 days postoperatively.

2 Nitrogen was spared in varying amounts in the majority of 21 gastric cases undergoing partial gastrectomy as compared to the nitrogen loss of six untreated controls. Eight other patients with miscellaneous conditions were studied and nitrogen sparing was produced in four.

3 Two previously healthy patients with severe fractures of the femur were maintained in nitrogen balance with a casein hydrolysate and high protein milk by mouth.

4 The nature of the reaction to injury is discussed and a simple hypothesis presented.

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## PART III

## CLINICAL RESULTS

IN THE PRECEDING PAPERS<sup>1, 2</sup> the suitability for clinical use of a mixture of pure amino acids has been established<sup>1</sup> and its effect upon postoperative nitrogen balance has been discussed.<sup>2</sup> Moreover, it has been postulated that the nature of the reaction of the body to injury, as far as nitrogen balance is concerned, is not solely upon anabolism, *i e*, antianabolism, or catabolism, but represents an increased stimulus to both, so that nitrogen equilibrium can be attained only at an increased level of nitrogen exchange. The present paper presents the clinical results from the high nitrogen intakes provided after operation by the use of the mixture of pure amino acids. Controlled observations of this sort are needed, since opinions vary considerably as to the value of high protein regimens after injury,<sup>3, 4</sup> and since few adequate reports of this nature are available.<sup>5</sup>

A type of surgical patient was selected for the present study, whose behavior after operation has been closely followed for many years, namely, ulcer patients subjected to partial gastrectomy\*. All of these were treated in a similar manner pre- and postoperatively, except that the pure amino acid mixture was given to half the patients. The procedures and methods are outlined in the preceding paper. The observations were carried out over the past one and one-half years.

## RESULTS

Twenty cases of peptic ulcer and one case of lymphoma of the stomach, without visible metastasis, were submitted to partial gastric resection and given the pure amino acid mixture during the immediate postoperative period. All were males. During this same period 29 cases of ulcer were similarly operated upon on the same division (L-floor) but were not given amino acid therapy. Nineteen of these were males. Age distribution, race, weight loss before operation, and the incidence of early ambulation were similar in the treated and control groups. These figures are presented in Tables VII, VIII, IX and X. The charts of 26 additional cases of partial gastrectomy for ulcer operated upon on another surgical division (K-floor) and in the Private Pavilion during the period of this study, are tabulated, for interest, as controls. They received no amino acids postoperatively but their treatment was not as uniform as in the control cases on the same surgical service as the amino acid-treated cases.

The choice of objective criteria by which to evaluate the results of amino acid therapy is greatly limited. The day on which the patient leaves the hospital,<sup>5</sup> the day after operation on which the temperature returns to normal, and the ability to progress with a postoperative diet provide data which can be compared with that of the controls and may be reasonably related to nitrogen intake. Also, a phenomenon of stasis and poorly functioning gastro-

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\* Dr F B St John kindly granted permission to study the cases on his Service

AMINO ACIDS IN SURGICAL NUTRITION

TABLE VII  
SHOWING AGE INCIDENCE

Age	Amino Acid- Treated	L-Controls	K-Controls	Private Controls
< 31	1	1	2	0
31 to 40	3	9	5	3
41 to 50	12*	11	3	7
51 to 60	3	5	5	
> 60	2	1	1	

\* One case of lymphoma

TABLE VIII  
SEX INCIDENCE IN RELATION TO DAY OF DISCHARGE FROM THE HOSPITAL AFTER PARTIAL GASTRECTOMY

Day Home Postoperative	Amino Acid- treated	L-Controls		K-Controls		Private Controls	
	Male	Male	Female	Male	Female	Male	Female
21 or before	19	17	4	8	4	6	2
22 or after	0	5	1	2	1	2	0
Died	2	0	1	1	0	0	0
Total	21	22	6	11	5	8	2

TABLE IX  
YEAR OF OPERATION IN RELATION TO DAY OF DISCHARGE FROM HOSPITAL  
AFTER PARTIAL GASTRECTOMY

Day Home Postoperative	Amino Acid-treated		L-Controls		K-Controls		Private Controls	
	July-Dec 1944	Jan-Sept 1945	July-Dec 1944	Jan-Sept 1945	July-Dec 1944	Jan-Sept 1945	July-Dec 1944	Jan-Sept 1945
21 or before	5	14	7	14	5	7	4	4
22 or after	0	0	3	3	2	1	0	2
Died	1	1	0	1	1	0	0	0
Total	6	15	10	18	8	8	4	6

enterostomy in postoperative gastrectomy cases occurring a week after the procedure may be observed since this complication may be nutritional in origin<sup>6</sup> Clinical impressions of strength and well-being are apt to lead to erroneous conclusions and only a statement about these is warranted, as a rule

*Day of Discharge* Table XI indicates the day of discharge after operation and indicates that 11 of the 54 control patients not receiving amino acids remained in the hospital 21 days or more The complications causing this delay are listed in Table XII Most of these may reasonably be related to inadequate nitrogen nutrition None of the 19 surviving cases treated with the amino acid mixture were kept beyond the 21st day In the untreated series, there were two deaths One was directly attributable to complications from operation, which may have stemmed from poor nutrition The other died of gas gangrene of the abdominal wall one day after operation, and, so, death was probably not precipitated by any nutritional factor In the treated series, there were also two deaths One resulted from peritonitis from an undiagnosed volvulus of the intestine, after four days of apparently good progress The other was also not attributable to protein depletion but may have died as the direct result of the amino acid administration This case is discussed in detail in the first paper of this series

TABLE X

NUMBER OF CASES ALLOWED EARLY AMBULATION IN RELATION TO DAY OF DISCHARGE FROM HOSPITAL AFTER PARTIAL GASTRECTOMY

Day Home Postoperative	Amino Acid treated		L-Controls		K-Controls		Private Controls	
	Amb	Not Amb	Amb	Not Amb	Amb	Not Amb	Amb	Not Amb
21 or before	15	4	13	8	9	3*	6	2
22 or after	0	0	4	2	2	1†	2	0
Died	1	1	0	1	0	1	0	0
	—	—	—	—	—	—	—	—
Total	16	5	17	11	11	5	8	2

\* One allowed up on day 6      † Allowed up on day 6

TABLE XI

DAY OF DISCHARGE AFTER PARTIAL GASTRECTOMY

Day Home Postoperative	Amino Acid treated		L-Controls	K Controls	Private Controls
	Adequate Rx	Inadequate Rx			
14 or before	8	3	8	4	2
17 to 15	2	1	8	6	6
21 to 18	5		5	2	
25 to 22			2	1	
30 to 26			1	2	1
40 to 31			3		1
Died	1*	1†	1	1	—
	—	—	—	—	—
Total	16	5	28	16	10

\* Volvulus      † Acidosis?

TABLE XII

TABLE SHOWING POSTOPERATIVE COMPLICATIONS IN PATIENTS NOT TREATED WITH AMINO ACID MIXTURE LEAVING HOSPITAL 21 DAYS OR MORE, AFTER PARTIAL GASTRECTOMY

Name	Floor	Age	Wt Loss before Oper (6 mos Day or less) Home	Postoperative Complications
I K	L	49	0	Died Subphrenic abscess day 4, with drainage Hemorrhage day 18 Jejunostomy day 25 to try to feed and raise plasma protein level of 4.46% Died day 25
J W	K	72	30	Died Gas gangrene abdominal wall and died day 1
T M	L	39	10	51 Distention marked to day 7 Perforated duodenal stump day 15 with exploratory operation Inability to void and cystitis throughout
A M	L	60	33	38 Pneumonia day 3 Parotitis day 7 Edema stoma and poor emptying (x ray) day 25 Wound ooze until discharge
M S	P P	45	10	34 Pulmonary infarct day 7 Vomiting and gastric residue day 21
J D	L	46	0	30 Repair perforated ulcer 37 days before partial gastrectomy Resection of ulcer 10 days before partial gastrectomy Pneumonitis day 3 and continued fever to day 14 after partial gastrectomy
N S	P	50	0	27 Soft distention to day 5 Vomiting with x-ray evidence of poorly emptying stoma day 12
A L	L	37	0	27 Pneumonitis day 4 Pulmonary infarct day 9 Renal pain left day 19
H S	K	56	0	26 Continued fever to day 15, with tender mass in RUQ spontaneously subsiding Cystic necrosis of omentum
M M	K	48	0	25 Continued fever to day 18 and pancreatic fistula day 6 on
L McD	L	43	0	24 Gastric retention with x ray evidence of edema of stoma and poor emptying day 11
J W	L	48	0	23 Jaundice day 5 Cephalin flocculation negative Alkaline phosphatase 7.9 B U plasma protein 5.3%
W C	L	39	10	22 Plasma protein 4.9% Gastric residue and vomiting to day 18

# AMINO ACIDS IN SURGICAL NUTRITION

TABLE XIII

SUMMARY TABLE SHOWING THE DAY OF DISCHARGE FROM HOSPITAL  
AFTER PARTIAL GASTRECTOMY

Day Home Postoper	Amino Acid- treated Cases	L-Controls	K-Controls	Private Controls
Day 21 or before	19	21	12	8
Day 22 or after	0	6	3	2
Died	2*	1	1	0
% > 21 days	0	19.2	20.0	20.0

\* Volvulus and acidosis

*Return of Temperature to Normal* The temperature after partial gastrectomy generally returns to normal by the 4th or 5th day after the procedure. In six of the 29 untreated cases, the fever did not subside until the 11th to 30th day. None of the amino acid-treated patients maintained a rise in temperature beyond the 11th day. This data is tabulated in Table XIV.

TABLE XIV

POSTOPERATIVE DAY WHEN TEMPERATURE RETURNED TO NORMAL  
AFTER PARTIAL GASTRECTOMY

Postoperative Day	Amino Acid- treated	L-Controls	K-Controls	Private Controls
1		1		
2	2			
3	11	1	3	
4	5	6	1	5
5	1	7	1	
8 to 6	0	4	3	
11 to 9	2	2	0	1
20 to 12	0	4	3	
> 20			1	
Died	2	1		

TABLE XV

POSTOPERATIVE DAY AT WHICH PATIENT COULD EAT  
A BLAND DIET AFTER PARTIAL GASTRECTOMY

Postoper Day	Amino Acid- treated	L-Controls	K-Controls	Private Controls
10 or <	4	2	5	3
15 to 11	15	18	7	5
20 to 16	2	2	2	
25 to 21		3		
Died	2	1	1	

*Abdominal Distention and Postoperative Edema of the Gastro-enterostomy Stoma* The incidence of these complications in the controls was definite, though perhaps too low to make comparisons significant. There were five cases of distention and five cases of late vomiting with gastric residue, in this group. Three of the latter five had roentgenograms to confirm the slow emptying and edema of the stoma. None of the treated cases showed these symptoms.

*Ability to Progress with a Postoperative Diet* Appetite and ability to eat a bland diet may have been improved by the amino acid therapy (Table XV). No instance of postoperative anorexia was noted in the treated series and all cases were able to add to their diet progressively. An ambulatory ulcer regimen, with 100+ Gm protein, was eaten, without objection, by day 12 after operation. The controls appear to have added foods to the diet almost as well as the treated cases, but the amount of food consumed was occasionally less than that provided by the diet. Figures relevant to intake are available in only 16 control cases, but show that five of the 16 were unable to keep up with their diet. It was noted that both the treated patients and the untreated controls with good appetite can progress much faster in respect to caloric and protein intake than the usual postoperative regimens permit.

*Well-being and Strength* The impression was gained that the treated patients were stronger than some of the controls, at the time of discharge. This point was not tested objectively.<sup>7</sup>

#### DISCUSSION AND CONCLUSIONS

There are three possible objections to forming final conclusions from the present study about the benefits to be derived from amino acid therapy after operation. First, the series is small. However, the cases are unusually uniform in respect to procedure, treatment, preceding weight loss, age, and the use of early ambulation.<sup>8</sup> Thus, minor differences may have more significance than in a larger but less homogeneous group. Also, the series is bigger than most of those from which conclusions have hitherto been drawn.<sup>5, 9, 10</sup> Second, only one-fifth of the control cases appear not to do as well as the treated ones. However, most of these patients are not severely protein depleted before operation so that, again, a slight change in recovery rate may be more significant than a similar small percentage in a more debilitated group. Third, the criteria used may not necessarily reflect protein depletion and repletion. The fact that both groups were identical except for the use of amino acids suggests that if there is any real difference in the behavior of the two groups, it must be the result of this one variable.

Despite the difficulties of evaluation, a positive influence of the treatment with the pure amino acid mixture is suggested by the data. Eleven of the controls stayed in the hospital considerably longer than any of the treated cases, and failed to restore their temperature to normal as quickly or to eat as well. Furthermore, five of these developed objective difficulties at the gastroenterostomy stoma, with gastric retention and roentgenographic changes, in the 2nd week after operation, whereas, none of the amino acid-treated cases showed this. Thus, a trial of this material in a larger number of patients appears warranted, to see if these results can be confirmed. Only uniformly treated and controlled groups of cases should be used, however, if useful data is to be obtained. Otherwise, the results cannot be interpreted. In any event, the results are not sufficiently distinct from those of the controls to indicate that routine unconsidered protein hydrolysate or amino acid therapy is necessarily of benefit.

Obviously, not all surgical patients will need a high nitrogen intake. The healthy individual has more than enough protein reserve to handle any acute injury. But where the drain on protein stores threatens to be protracted, as after fracture, or has been severe as with burns, repeated trauma or infection, such therapy seems indicated to conserve nitrogen and to avoid the complications of protein depletion,<sup>11-14</sup> if possible.

The question then arises as to whether the best procedure is to force nitrogen intake before or after operation, or at both times. Positive nitrogen balance is produced readily before injury, but with difficulty afterwards, so that there is no doubt that the preoperative period should be used to full advantage. However definite amounts of nitrogen can be spared to the body after injury in many patients. Thus, if body nitrogen stores have been depleted by weight loss, gastric retention, anorexia, hemorrhage, secondary operation or infections<sup>15</sup> before or after operation or injury, a high nitrogen regimen is indicated after the procedure, as well as before.

If such a regimen is desired either before or after operation, the ability to eat and retain food becomes important. A practicable parenteral regimen has been outlined<sup>2</sup> which meets body nitrogen requirements by the use of mixture of pure amino acids and glucose-saline solution, when the patient cannot take nourishment by mouth. Nausea, acidosis, low calories and the large volumes of fluid required are the difficulties encountered, although sodium lactate ( $\frac{1}{6}$  molar) solution and a rate of administration of 400 cc per hour of the 8 per cent amino acid solution generally prevent the first two of these complications. The wastage of nitrogen by this method is high, so that 20-28 Gm of nitrogen may be needed to insure nitrogen sparing for most patients. But nitrogen is spared, especially in the debilitated patient in whom significant nitrogen loss is undesirable.

However, when some food can be eaten, the amino acids find their most efficient use, namely, to supplement an inadequate intake to achieve a normal or high nitrogen level. The equivalent of 60 Gm of protein can be given in a liter of fluid, in a 2.5-hour period, and most of this nitrogen is retained.<sup>2</sup> Incidentally, the infusions produce anorexia for several hours, so that the end of the day, after the patient has eaten, is chosen for the infusion, which is brief enough not to interfere with sleep.

Mention must be made of the work on high carbohydrate and high caloric intakes in sparing nitrogen after injury.<sup>16</sup> These regimens require very large intakes of food. If this can be achieved, with moderate nitrogen intake, there is no reason why this method should not be used. If the patient cannot eat the required amounts, the high nitrogen regimens discussed above are simpler and more practicable and will spare protein when needed.

#### SUMMARY

1. A clinical study has been made of the effect of postoperative treatment with a mixture of pure amino acids on the recovery from partial gastrectomy.

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The author is greatly indebted to Dr. Allen O. Whipple for his advice and continued interest in the entire project.



of 21 ulcer patients, as compared to 32 similar cases handled in the same way but not given the amino acid mixture

2 A fifth of the controls appear to do less well than the amino acid-treated cases. However, the results in the two groups are similar enough to raise the suspicion that routine, unconsidered postoperative therapy with hydrolysates or amino acids may be in large part unnecessary

3 The criteria of clinical benefit used are evaluated as are the indications for high nitrogen intakes before and after operation

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# THE CLINICAL BEHAVIOR OF ARTERIOSCLEROTIC ANEURYSM OF THE ABDOMINAL AORTA A RATIONAL SURGICAL THERAPY

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IN A GROUP of 32 cases of aneurysm of the abdominal aorta admitted to the Presbyterian Hospital in recent years, arteriosclerosis was the cause of the aneurysm in 26. These aneurysms were fully developed, fusiform in shape and arose from the abdominal aorta three or more centimeters distal to the origin of the renal arteries. Syphilis was the etiologic agent in six of the 32 cases, these aneurysms being saccular and causing vertebral bone erosion in four instances. In this latter group the aneurysm arose distal to the renal arteries in only one of the six cases. There were only two females in the entire group of 32 cases, both having arteriosclerotic aneurysm, and the average age of those with arteriosclerotic aneurysm was 60 years while it was 42 years for the syphilitic group.

One gains the impression from the literature that there is a high incidence of vertebral erosion in aneurysm of the abdominal aorta but such was not the case in the arteriosclerotic group of our series. Of the 26 cases of arteriosclerotic aneurysm, vertebral erosion was noted in only one instance, and in this case, erosion was due to aneurysmal involvement of the right common iliac artery. Aside from the fact that the arteriosclerotic aneurysm is usually fusiform, it seems likely there may be another factor accounting in part for the rarity of bone erosion, namely, elongation of the abdominal aorta. Considerable elongation of the vessel seems an invariable precursor to the formation of the arteriosclerotic aneurysm of the abdominal aorta. In fact, a study of many specimens reveals, a few centimeters below the renal arteries, a sudden change in direction of the aorta, (usually forward, but often to the left or right), and immediately distal to this angulation the fusiform aneurysm begins. It is common at operation to note an angulation of the aorta sometimes as much as 90 degrees immediately proximal to the origin of the arteriosclerotic aneurysm, the latter scarcely touching the vertebrae. What may be the added effect upon angulation by flexion of the thoracolumbar spine is a matter of conjecture, and, of equal importance, the hemodynamic water hammer effect of strain upon the lower abdominal aorta consequent to angulation of the sclerotic iliac arteries by flexion of the thighs as in the sitting position. We speak of angulation of the arteriosclerotic artery in the sense of its walls buckling rather than bending with a gentle curve, as would a normal artery.

We know from experimenting with arteriosclerotic popliteal arteries that flexion angulation causes a water hammer effect of increased strain upon the popliteal artery lying immediately proximal, unsupported in the upper popliteal space. In our opinion, this is an important factor in the development of

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arteriosclerotic popliteal aneurysms and it seems likely that a similar mechanism may play a part in the development of the arteriosclerotic aneurysm of the lower abdominal aorta. As possibly having some bearing on the above discussion, it is of interest that, as far as our hospital service is concerned, the popliteal artery and the lower abdominal aorta are the common arteries affected by arteriosclerotic aneurysm. By this we mean well-developed aneurysms—not counting, of course, dissecting aneurysms of the sclerotic thoracic aorta.

As may be expected, the difference in pathology between the syphilitic and arteriosclerotic aneurysm of the abdominal aorta, as pertains to vertebral erosion, affects the incidence and severity of pain. Thus, the four syphilitic cases with vertebral erosion had for months received opiates for the control of severe radicular pain. Complete relief of pain following wiring and electrothermic coagulation of the aneurysm could only mean that the aneurysm became smaller in size following operation, thus, relieving pressure upon the spinal nerves. Unfortunately one of the four cases having a subluxation of the vertebrae died of infection following a bone graft procedure done some months after the wiring operation. The remaining three cases are alive, active and pain free now, eleven, seven and four years, respectively, following operation.

One gains the impression from the literature that the high incidence of vertebral erosion with resultant radicular (nerve pressure) pain is so constant in aneurysm of the abdominal aorta as to constitute a diagnostic sign. Our attention is called to the fact that vertebral erosion was present in only five of the 32 cases herein reviewed and in only one of the 26 cases in which the aneurysm was due to arteriosclerosis. This suggests, that in the past medical literature of the symptomatology of aneurysm of the abdominal aorta has been built up largely from syphilitic cases—cases which give a long drawn out history of severe pain due to nerve pressure from bone erosion.

Pain is the most important symptom that makes people seek medical relief. Due to the absence of bone erosion as an early cause of pain in the arteriosclerotic aneurysm of the abdominal aorta, the unfortunate victim of this disease often goes to the brink of disaster before seeking medical aid. A recent case illustrating this may be outlined as follows. A local physician called, stating that five days previously he had seen, for the first time, a 64-year-old man who gave a history of having, from time to time, for several months, a slight pain in the low back, including the sacro-iliac regions. The pain was exaggerated by bending forward or by exertion. Suddenly the pain became intense, radiating to the posterior aspect of the legs. Three days after onset the pain had extended up the back, over the abdomen, into the groins and down the anterior aspect of the thighs. On the fourth day of onset the patient began to vomit. When I saw the man, two days later (on the 6th day of his illness) he was under the influence of sedatives, pulse 84, B P 120/60. He appeared anemic but not in shock. The skin was warm and dry. The abdomen was not soft but neither was it distended with gas. A large, pulsating mass was present in the region of the abdominal aorta. The scrotal and perineal tissues were ecchymotic. An hematocrit made at this time was 23.8.

This man undoubtedly had had a large arteriosclerotic aneurysm of the abdominal aorta for months before having what he considered sufficient symptoms to warrant seeing a doctor. His first real nerve pressure pain comparable to the radicular pain of early bone erosion in the syphilitic case was actually caused by rupture of the aneurysm resulting in a spreading retroperitoneal hematoma.

Essentially, the story of pain from the beginning rupture of the aneurysm as the presenting symptom of consequence was elicited in 11 of the 26 cases of arteriosclerotic aneurysm. Some of the cases came under medical care with the history of less violent and more varied initial symptoms. Loss of weight is a common complaint in arteriosclerotic, as is the case with syphilitic aneurysm of the abdominal aorta. Eleven of the 26 cases of arteriosclerotic aneurysm had sustained weight losses varying from 15 to 35 pounds.

In five of the 26 cases of arteriosclerotic aneurysm a pulsating mass in the abdomen first directed attention to a diagnosis.

A sudden episode of severe, cramp-like abdominal pain, followed by collapse, was the apparent symptom of onset in a 51-year-old physician in whom, four months later, a well-developed fusiform arteriosclerotic aneurysm was palpable.

Severe hunger pains, combined with anorexia, punctuated the symptoms in another case—a man of 55, in which the aneurysm had been observed to grow to the size of a large grapefruit over a three and one-half-month period.

Our oldest case, a man of 72, had attacks lasting several days, which simulated ileus or duodenal obstruction. One of these attacks complicated our second-stage wiring operation. The old gentleman recovered, following Miller-Abbott intubation, however, and lived some two years, finally dying of a cerebral accident. Considering the great amount of forward displacement of the third portion of the duodenum, often seen in cases of large aneurysms, one marvels at the relative infrequency of symptoms of duodenal obstruction. Postoperative edema does add to this hazard, however, and in one other case we considered it a contributory cause of death. Again, contrary to what one would expect, in the relation of the transverse colon to a large aneurysm of the abdominal aorta, we have been surprised at the rarity of bad constipation.

We may close the discussion on the symptomatology of arteriosclerotic aneurysm of the abdominal aorta with a word of warning about pain. Analysis of the 26 cases of arteriosclerotic aneurysm affords convincing evidence that the appearance of deep-seated abdominal pain, low back pain and pain radiating to the hips or legs is a warning of impending disaster. Furthermore, my experience has been that the mortality of well-developed arteriosclerotic aneurysm of the abdominal aorta is quite as great as that of syphilitic aneurysm.

#### THE SURGICAL TREATMENT OF ANEURYSM OF THE ABDOMINAL AORTA

The ideal surgical therapy for degenerative arterial aneurysm entails cure of the aneurysm with maintenance of the arterial blood flow through the vessel affected. Whereas the above ideal has been successfully accomplished in

so-called peripheral aneurysm, in aneurysm of the aorta, where it has been considered essential to preserve arterial blood flow, we have been forced to rely upon blood clotting within the aneurysmal sac as our main bulwark against the continued growth of the lesion

In the year 1935, with the valued aid of Professor Barry G King, of the Department of Physiology of the College of Physicians and Surgeons, a series of investigations in the hemodynamics of aneurysm was begun. In the first place, when the yellow elastic tissue of the aorta wall is destroyed and the media gives way, the budding aneurysm is subjected to a strain which increases *pari passu* with its growth. Blood, circulating under pressure, creates a strain on the sac wall of an aneurysm varying with the square root of its surface area and, to a lesser extent, with the rate of blood flow. Doubling the diameter of the aneurysm, for example, increases the strain on the sac 100 per cent. The stretched sac is further devitalized due to failure of blood supply to the sac wall to keep pace with the expanding sac. Thus, there is a vicious circle in a growing aneurysm of increased strain upon a sac wall of diminishing strength.

On the other hand, clotting of an aneurysm does offer the advantage of the physical laws governing solids. To illustrate: when the fluid blood of a saccular aneurysm becomes a solid, the total strain upon the aneurysmal sac wall is reduced from the aggregate pressure exerted on the total surface area of the sac wall to that of the pressure exerted on the surface area of the mouth of the aneurysm only. The true magnitude of this reduction in strain is only fully appreciated when one stops to consider that the surface area of the mouth of the saccular aneurysm is usually but a small fraction of the total surface area of the sac wall. It is not surprising, then, in accordance with the above mentioned physical laws, that authentic instances of nature's cure of saccular arterial aneurysm have accumulated in the literature of pathology for over 100 years—cases in which clotting of the aneurysm had resulted in complete inactivation of the lesion—the patients having subsequently died of some other cause. It is but reasonable to assume that removing the strain upon the sac wall, caused by the expanding pulsations of fluid blood, by converting the blood to a solid blood clot affords the strengthening processes within the sac wall an opportunity to become effective.

Our studies revealed that the initiation and propagation of mass clotting within aneurysms is dependent largely upon two important factors: namely, (1) the presence of adequate stimulus to blood clotting, and (2) the rate of blood flow through the aneurysm. We have obtained rate of blood flow measurements in approximately 150 aneurysms. It is of extreme importance to note the great variations in the rate of blood flow. For example, in two saccular aneurysms of equal size the rate of blood flow through the aneurysm may vary as much as 300 per cent. The larger the mouth of a saccular aneurysm the higher the rate of blood flow through the aneurysm. In cases of so-called "cup-shaped" saccular aneurysms in which the diameter of the mouth of the sac is equal to, or exceeds, the diameter of the sac, the rate of blood flow

through the aneurysm is extremely rapid—approximating that of fusiform aneurysms

One may correlate the relation of the rate of blood flow to spontaneous clotting within aneurysms by simply reviewing pathologic specimens. It is rare, indeed, to find any appreciable deposit of blood clot within fusiform or wide-mouth saccular aneurysms.

Thus, we see that nature's cure of aneurysm has been relegated usually to the occasional case of small-mouth saccular aneurysm in which conditions favor complete "brimful" clotting of the aneurysm.

The first attempts to induce clotting within aneurysm by the introduction of wire date back to Moore, in 1864. Fifteen years later, Corradi suggested the use of an insulated needle through which to pass silver wire into the aneurysm. The protruding end of bare wire was then connected to the positive pole of a battery, the negative electrode was applied to the skin in the neighborhood and a galvanic current passed. The resulting ionization product deposited at the surface of the wire was depended upon to encourage the initiation of blood clotting within the aneurysm. Subsequently, Colt advocated the introduction of multiple wisps of wire into aneurysms to act as a nidus for the initiation of blood clotting. A thorough review of published cases employing these wiring methods revealed a great uncertainty in the results with an occasional brilliant success. Now that we know of the great variation in the rate of blood flow in aneurysms and the relation of rate of blood flow to blood clotting, we can readily understand their results.

We now have conclusive experimental and clinical evidence that a method of wiring aneurysms to be efficient in the induction of mass (brimful) clotting must fulfill the following requirements: (1) it must afford an adequate and efficient clot-stimulating surface to the passing blood, and (2) it must furnish a means of measuring blood flow in the individual aneurysm as a guide to the amount of wire it is necessary to introduce to impede the blood to a rate of flow at which, in the presence of an adequate clot-stimulating surface, complete mass clotting of the aneurysm will take place.

#### METHOD

The electrothermic method of coagulating aneurysms embraces the use of fine (34-gauge B & S), insulated, coin silver wire sterilized by autoclave. The wire is introduced into the aneurysm in ten-meter segments through a special needle (Fig 1). Five meters of wire are wound on each of two aluminum spools and bent into a loop in the middle for passage through the needle. This permits the two ends of the segment of wire to protrude from the needle for the purpose of establishing electrical contact.

A source of approximately 100 volts of direct current is used for the heating apparatus (Fig 2). The current is so regulated (Fig 3) and calibrated against changes in the electrical resistance of the wire upon heating as to show an accurate measurement of the temperature of the wire on a ratiometer at all times and of the rate of blood flow through the aneurysm upon initial heating. Each ten-meter segment of wire is finally heated to 80° C for

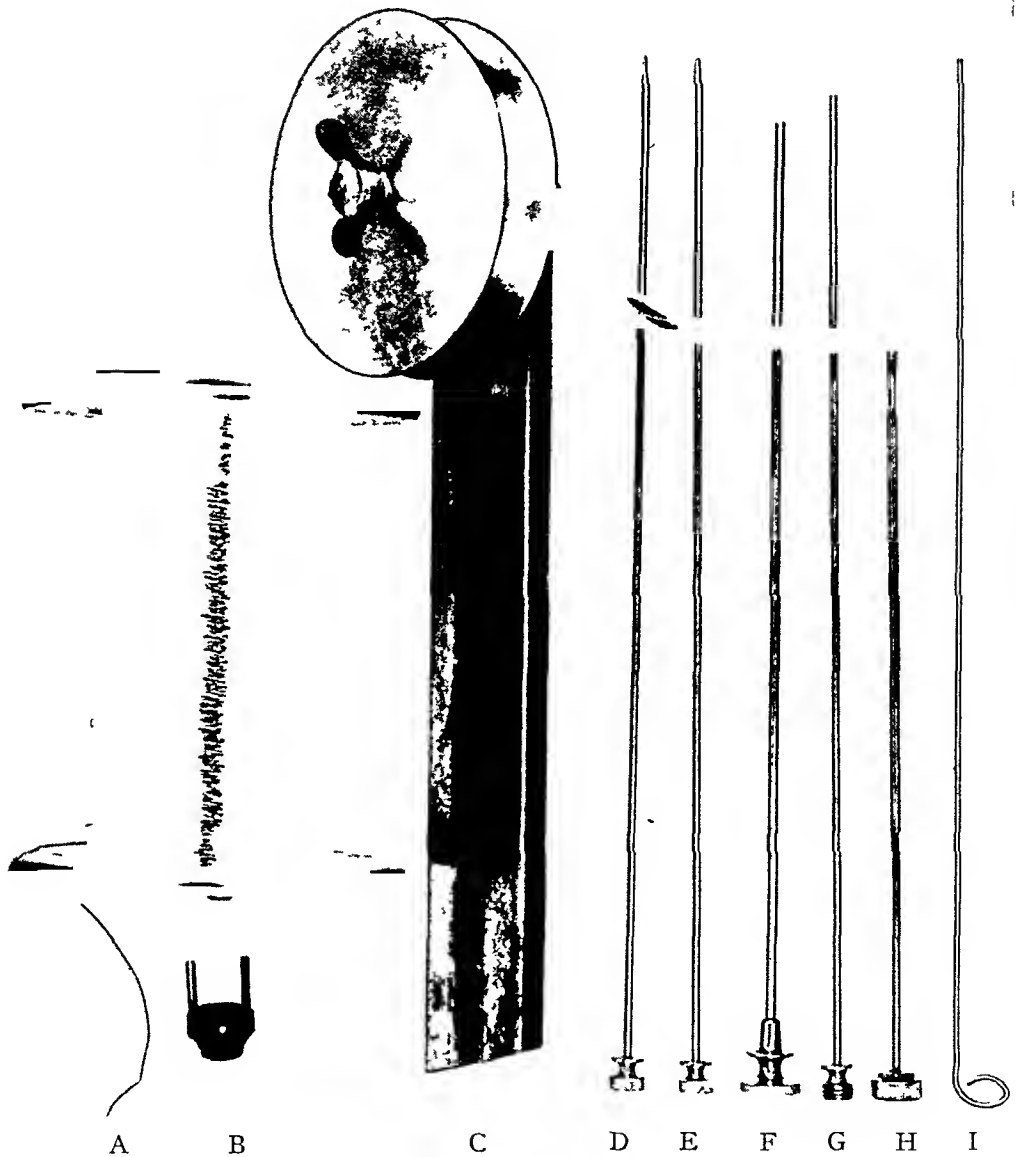


FIG 1—Armamentarium for Coagulating Aneurysm

(A) Enameled wire on spool, (B) electrode cap, adapted to (G), (C) hand reel for winding wire on spools, (D) a trocar-pointed stylet adapted to (F) for traversing firm tissues and piercing the sac of the aneurysm, (E) tapered blunt stylet adapted to (F) for traversing tissue of lung, (F) 14-gauge, 6 1/2 in needle made of stainless steel, with the end beveled from without in, (G) inner sheath for needle (F) which locks in place and has the end beveled from within out, fitting exactly with needle (F) to furnish a rounded nonabrasive end, (H) wire-passer adapted to (G), and (I) a blunt stylet adapted to (G)

a ten-second period. This results in the deposit of a tenacious, clot-stimulating, protein coagulum upon the wire.

On the basis of the number of amperes of current required to heat the first ten-meter segment of wire introduced into the aneurysm it is possible to determine the following: (1) the variety of aneurysm (based upon rate of blood flow), and (2) approximately the number of segments of wire it will be necessary to introduce into the aneurysm to impede the blood flow to the point of occurrence of mass clotting, namely, the requirement of three amperes to raise the temperature of a final segment of wire to  $80^{\circ}\text{C}$ .

To avoid the occurrence of "hot spots" upon heating and to promote a more even distribution of protein coagulum upon the wire throughout the segment it is desirable to attain an even distribution of the wire within the aneurysm. This is greatly facilitated by mounting the two spools upon a geared reel which,

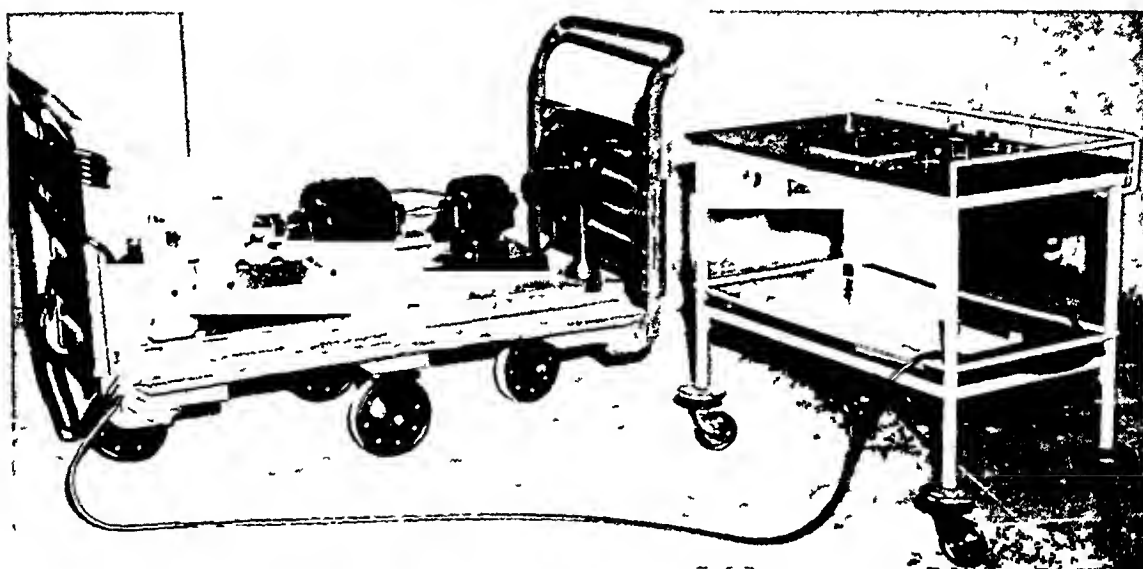


FIG 2—Photograph of alternating to direct current converter and heating control panel

when turned by an assistant during the introduction of the wire, rotates the spools in opposite directions. This, in turn, twists the two wires in opposite directions, forcing them apart upon gaining the inside of the aneurysm. The wire has sufficient expansile thrust when combined with the torque imparted to the wire by the geared reel, to serve to distribute it evenly through the aneurysm.

#### TECHNIC

Rigid asepsis directed against air-borne as well as direct bacterial contamination must constantly be kept in mind. In cases in which a direct surgical approach is not made to expose the aneurysm, the operation is done under novocaine infiltration anesthesia with roentgenologic guidance. It is now considered best to introduce the needle through a skin incision using towels over the skin edge held in place by skin clips. All instruments used to this point are discarded and gloves are changed before proceeding with the operation. The special needle (Fig 1, F), is introduced through the sac wall of the



aneurysm, using the sharp trocar-pointed stylet (Fig 1, D) The trocar-pointed stylet is replaced by the special inner sheath (Fig 1, G) bearing a blunt stylet (Fig 1, I) A loop of wire is passed through the wire-passer (Fig 1, H), which, for the time, is left unattached to the needle Adequate wire is unwound from the spools mounted upon the geared reel The loop of wire is then advanced through the needle to a point two or three centimeters beyond the end of the needle The operator holds one wire and advances the other, thus, forcing the formation of the first loop of wire within the aneurysm Next, the wire that has been held is gently withdrawn until the bend in the wire snugs-up to the end of the needle This assures one that the loop thus formed and subsequent loops will land within the sac of a saccular aneurysm After the passage of several loops of wire by hand, the wire-passer is attached to the needle and the wire quickly passed two wires at a time The introduction of a ten-meter segment of wire requires about five minutes

ELECTRICAL HEATING OF WIRE IN ANEURYSM  
BLOCK DIAGRAM OF CIRCUIT

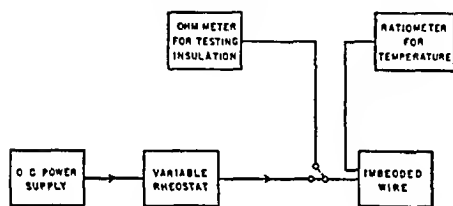


FIG 3—Diagram of electrical circuit

if any The insulation of the wire is tested before heating, (see ohmmeter, Fig 3) The rate of blood flow through the aneurysm is next measured by noting the number of amperes required to raise the temperature of the wire  $15^{\circ}\text{C}$ , i.e., an average temperature of  $53^{\circ}\text{C}$  The wire is finally heated to  $80^{\circ}\text{C}$  for a period of ten seconds After an interval the wire may be reheated for another ten-second period Finally, the wire is clipped flush with the needle and the ends pushed into the aneurysm with a blunt stylet (Fig 1, I) Additional segments of wire are introduced and heated until a final ten-meter segment requires three amperes to raise the temperature of the wire to  $80^{\circ}\text{C}$  Experience has revealed that when one or more segments of wire, well-distributed within a saccular aneurysm, requires only three amperes to heat the wire to  $80^{\circ}\text{C}$ , mass clotting of the aneurysm takes place at once It has been a routine policy at the final operative stage to check the completeness of clotting by making an arteriogram

Since the rate of blood flow through aneurysms of similar size may vary as much as 300 per cent, the amount of wire necessary to impede blood flow to a point conducive to mass clotting must likewise vary greatly Each ten-meter (33-foot) segment of wire has a surface area of eight square inches The deposit of a layer of protein coagulum by heating increases the surface area to approximately 16 square inches Some idea of the magnitude of the clot-stimulating surface exposed to flowing blood and the impedance to blood flow effect

may be obtained by multiplying the above figure by ten, the number of ten-meter segments often required to obtain mass clotting in wide-mouth, high rate of flow aneurysms

Adherence to the wire and to the sac wall of a clot deposited within an aneurysm is imperative and its organization desirable. Whereas wire alone may reinforce blood clot, the heating to  $80^{\circ}\text{C}$  of wire distributed on the inside surface of an aneurysm sac, as above advocated, causes inflammation in the sac wall. Tissue subjected to a temperature of  $80^{\circ}\text{C}$  for a few moments reacts within 24 hours with edema, vascular engorgement, and a typical inflammatory reaction on the part of the white corpuscles. The peak of the heat inflammation is reached in from four to six days. This is followed by a period of repair, in which fibroblasts appear and tissue organization takes place with the aid of a network of budding capillaries. The entire reaction occupies a period of from ten to twelve days without, at any time, the appearance of tissue slough. Experimental and clinical evidence suggests that inflammation as engendered by the electrothermic method of wiring aneurysms is an important factor in strengthening the sac wall of an aneurysm.

The electrothermic method has enabled us to attain "brimful" clotting of wide- as well as small-mouth aneurysms. Extensive clotting has been attained in high blood velocity fusiform aneurysms and in a few instances the channel available to blood flow through the aneurysm has been narrowed to approximate the diameter of the parent aorta. A fair number of cases of wide-mouth saccular aneurysms due to syphilis treated by wiring and electrothermic coagulation has now been followed for periods in excess of five years (one case ten years) without showing any return of preoperative symptoms or roentgenographic evidence of increase in size. However, a statement of physical fact was made that "brimful" clotting of saccular aneurysms reduces the strain upon the sac to that resulting from the lateral wall pressure upon the surface area of the mouth of the aneurysm only.

Since the strain is in proportion to the surface area of the mouth, other things being equal, a fully clotted, wide-mouth saccular aneurysm is subjected to a greater strain than a fully clotted, small-mouth saccular aneurysm, and, by the same token, a well, but not completely clotted, fusiform aneurysm is subjected to more strain than a "brimful" clotted wide-mouth saccular aneurysm. As would be expected from these physical facts, our results have indicated that we may expect permanent inactivation in cases of saccular aneurysm belonging to the smaller-mouth group in which "brimful" clotting may be attained (longest follow-up 11 years). Some of the wide-mouth syphilitic saccular aneurysms, however, have remained stabilized for several years, only to manifest evidence of gradual reactivation. A few of these were subjected to another wiring operation with remarkable palliation of symptoms. The wiring and electrothermic coagulation method has given a new lease on life to many cases of fusiform syphilitic aneurysm of the aorta. Many of the cases were stabilized for 4-, 6- and 8-year periods, during which they were in the great part symptom-free from shrinkage of the aneurysms following operation.

Early in our experience with wiring and electrothermic coagulation of the arteriosclerotic fusiform aneurysm of the abdominal aorta we appreciated that less inactivation of the aneurysm resulted from a given amount of clot deposited than obtained in a similarly-treated syphilitic fusiform aneurysm. This lack of resistance to expansion of the aneurysm sac is not unexpected when one considers that arteriosclerotic degeneration is likely to involve the entire thickness of the aorta wall.



FIG. 4—Roentgenogram of arteriosclerotic aneurysm of the abdominal aorta in a man age 55

The fusiform aneurysm with the aorta has been occluded with wire, using the method of electrothermic coagulation and endo-arterial occlusion. The collateral circulation is adequate.

Whereas, it seemed certain that clotting the arteriosclerotic fusiform aneurysm down to a narrow channel did slow up the rapidity of growth of the aneurysm, a complete cure could only be counted upon if all blood ceased to flow through the aneurysm. The above conclusion was gradually arrived at through an experience with several cases over a 2- to 4-year period.

As previously stated in our group the arteriosclerotic aneurysm arose from the abdominal aorta some three, or more, centimeters distal to the origin of

the renal arteries in all of the cases examined. This is a fortunate finding because, following wiring with the deposit of clot within the aneurysm, there is one obstacle to hurdle to attain a cure of this vicious lesion, namely, a safe and sure way of occluding the arteriosclerotic abdominal aorta. A critical review of the total surgical experience recorded of ligation of the abdominal aorta prompted the late Dr. Mont R. Reid<sup>1</sup> to state that "partial or gradual occlusion of the aorta by compression (constriction) cannot succeed and should not be attempted. This applies also to the use of partial constrictions proximal to a totally occluding ligature." Brooks, Blalock and Johnson<sup>2</sup> have pointed out that the immediate mortality and incidence of gangrene is so high in humans as to preclude the use of a one-stage occlusion of the aorta.

An experience with some five cases of arteriosclerotic aneurysm in which gradual compression (constrictive) occlusion of the aorta was practised in conjunction with wiring and electrothermic coagulation of the aneurysm convinced me of the wisdom of Doctor Reid's remarks. A possible safe way of securing gradual occlusion of the aorta suggested itself to us in treating four cases of arteriosclerotic aneurysm of the popliteal artery by wiring and electrothermic coagulation. This was before the days of controlled anticoagulant therapy and the wiring method was decided upon because the collateral circulation was poor in these cases. The fusiform aneurysms were gradually and progressively occluded and with them the popliteal arteries, in two or three operative stages, in these four cases without mishap. This experience proved two things: (1) that in the electrothermic method we had a way of obtaining controlled blood clotting, and (2) the impedance effect of wire introduced into the popliteal artery afforded a means of gradual occlusion of the artery from within, without interference with the blood supply to the artery wall.

We thought it fitting to try this principle of endo-arterial occlusion first on a case of arteriosclerotic aneurysm of the abdominal aorta who had restored an essentially normal blood flow through the aneurysm because of cutting through of a cotton tape which had been placed upon the aorta some months previously. Not only had the tape cut through the aorta wall for most of its circumference but there was at the band site a thin-walled aneurysm, the size of a plum. First, a 33-foot segment of insulated wire was introduced into the secondary (traumatic) aneurysm and heated to 80° C. Following this, some 150 feet of No. 34-gauge (B & S) coin silver wire coated with partly hydrolyzed polyvinyl acetate was forced into the abdominal aorta immediately proximal to the beginning of the aneurysm but distal to the origin of the renal arteries. The wire was concentrated in a ball obstructing the aorta to the desired amount using the oscillogometer on the leg as an indicator. Partly hydrolyzed polyvinyl acetate coating of the wire was employed primarily for its tissue-irritating effect in stimulating fibroplasia through the meshes of the wire. If this effect is not desired, *e.g.*, in a first-stage partial closure, bare wire may be employed. The combined principle of using unheated wire for gradual occlusion of the aorta immediately proximal to the origin of the aneurysm and

heated (insulated) wire directly in the aneurysm was successfully carried out in this case and it is now some three years since operation. The combined method of endo-arterial occlusion and electrothermic coagulation has now been employed successfully in three cases of fusiform arteriosclerotic aneurysm of the abdominal aorta and two cases of syphilitic fusiform aneurysm of the abdominal aorta. It is unnecessary to emphasize the necessity of using a method of inducing clotting within the aneurysm in which control of the amount of clot induced at a given time is possible. After a thorough investigation of the methods of creating clot-stimulating surfaces upon wire (electrolysis, protein coatings from blood, gelatin, *etc.*), we concluded that electrothermic coagulation, according to the technic described, is the only method which affords selective, controlled clotting within aneurysms. The electrothermic method gives selective clotting following the introduction and heating of a given amount of insulated wire simply because the clot-stimulating protein coagulum is deposited only upon those portions of the wire within the recesses of the sac of the aneurysm. Wire thus located becomes heated and, thus, coated with protein coagulum because it is not exposed to the cooling effect of the faster moving blood in the axial current. This important underlying characteristic of the electrothermic method of wiring aneurysms makes it peculiarly suited to use in combination with endo-arterial occlusion in the gradual obstruction and clotting of the parent artery with the aneurysm in those cases of aneurysm in which sudden occlusion would mean the loss of life or limb.

#### SUMMARY

Some important differential features in the pathology and symptomatology of aneurysm of the abdominal aorta due to syphilis and arteriosclerosis are brought out in a review of 32 cases. Arteriosclerosis was the cause of the aneurysm in 26 of the 32 cases reviewed.

The importance of pain as a warning of beginning rupture with spreading retroperitoneal hemorrhage in cases of arteriosclerotic aneurysm was emphasized. Attention is called to the fact that there is almost invariably an interval of from two to six days following beginning retroperitoneal hemorrhage before death supervenes from sudden rupture of the retroperitoneal hematoma into the general peritoneal cavity—a period during which life-saving measures may be instituted.

A method of wiring and electrothermic coagulation of aneurysms is presented and discussed. A technic is described for the surgical cure of fusiform aneurysm of the abdominal aorta employing wiring and electrothermic coagulation in conjunction with gradual endo-arterial occlusion.

#### CONCLUSION

It seems certain, due to the tremendous decrease in mortality from pneumonia and some other diseases, that formerly took great toll in people of the arteriosclerotic age-group, that the surgical therapy of the arteriosclerotic

aneurysm of the abdominal aorta will assume a position of increased importance

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# INTRAVENOUS OXYGEN AND PULMONARY EMBOLISM

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IN A RECENT STUDY by Jacoby *et al*,<sup>1</sup> on the effects following the intravenous administration of oxygen to dogs and human beings, it appeared that this form of therapy may have an important place in the treatment of shock. They pointed out that undesirable effects of pulmonary embolism or cardiac tamponade in previous studies were due to the administration of too large a quantity of the gas or to the injection of the gas at too high a pressure. However, in our experience, as reported herein, we could not demonstrate any significant benefit following intravenous oxygen, on the contrary, in some instances definite deleterious effects were noted.

A review of the literature reveals that extrapulmonary respiration was attempted as far back as 1811.<sup>2</sup> Tunnichiffe and Stebbings,<sup>3</sup> in 1916, Singh and Shah,<sup>4</sup> in 1940, injected oxygen intravenously to human beings who were suffering from anoxia of various causes. They reported excellent clinical improvement in each case. Bouine and Smith,<sup>5</sup> in 1927, Dick,<sup>6</sup> in 1929, and Grodins, Ivy, and Adler,<sup>7</sup> in 1943, all administered intravenous oxygen to dogs at various rates. They found that intravenous oxygen caused pulmonary embolism and a distinct arterial hypoxemia. Contrary to these findings, Jacoby described experiments on dogs in shock to whom intravenous oxygen was of distinct benefit. Similarly, he described three human patients in shock who showed marked clinical improvement with intravenous oxygen.

Inasmuch as it appeared possible that intravenous oxygen may be of benefit to patients in shock, it was decided that further study was indicated especially in regard to the changes in the oxygen saturation of arterial blood.

## METHODS AND PROCEDURES

The method used to administer the oxygen was by water displacement of the gas from a gallon container to a wash bottle, and from thence by tubing to the patient. By means of a Murphy-drip system and a water manometer attached to the top of the wash bottle, small but accurate rates of oxygen at known low pressures could be delivered for several hours at a steady flow. A cubital vein was used as the site of the oxygen injection on all patients. Van Slyke gasometric analyses of the oxygen content of arterial blood were done on blood samples drawn from a femoral artery with oiled syringes. At least two samples were drawn for each determination. Hemoglobin determinations were done with a photometer. Oxygen capacities were calculated therefrom. Blood pressure, pulse, respirations, and hematocrits were recorded at regular and frequent intervals. Electrocardiographic tracings were taken on two

patients, and a series of roentgenograms of the chest on one patient. All these various determinations were done before oxygen was administered and while the gas was given at different rates intravenously. Experiments were conducted on four postoperative patients, all of whom were considered stable from a cardiorespiratory viewpoint. In addition, two patients in shock were also studied. Finally, an *in vitro* experiment was performed in which oxygen was passed through 50 cc of venous blood at various rates to note any changes in oxygen saturation of the blood.

#### CASE REPORTS AND RESULTS

**Case 1**—Studies were done on four stable, conscious patients. The first of these was a 60-year-old white laborer, upon whom a celiotomy had been performed three days previously. At this time a diagnosis was made of inoperable carcinomatosis of the liver of unknown origin. His laboratory findings included a red blood cell count of 3,600,000, hemoglobin 9.3 Gm, and total blood proteins 4.2 Gm per 100 cc. He was afebrile, very jaundiced, and had a pitting edema of his ankles. Blood pressure 105/65, respirations 15, and pulse 72. The arterial oxygen saturation decreased from 94 per cent to 55.5 per cent after the administration of 9.3 cc of oxygen per minute for 20 minutes. It then further decreased to 46 per cent saturation at the slower rate of 6.6 cc per minute for 12 minutes. The rate was decreased because of the onset of symptoms which appeared 15 minutes after the patient had received oxygen at the rate of 9.3 cc per minute. These symptoms consisted of a sensation of pressure in the lower chest, cough, restlessness, and profuse perspiration; some relief was obtained by placing the patient in Fowler's position. Symptoms lasted until 13 minutes after the oxygen was stopped. Respirations increased from 15 to 23, pulse and blood pressure remained constant.

**Case 2**—This patient was a 68-year-old colored laborer. A partial gastrectomy for chronic peptic ulcer had been performed five weeks previously. Postoperatively, he developed an abscess and gangrene of the lower lobe of his right lung. At the time of this study, he was afebrile and showed a distinct cyanosis of his lips. His pulse was 78, respirations 20, and blood pressure 120/90. The laboratory findings revealed a red blood cell count of 4,300,000, hemoglobin 13.8 Gm, and total proteins 5.2 Gm per 100 cc. His radial and femoral arteries were very sclerotic. The arterial oxygen saturation at the onset was only 77 per cent, which low value we attribute to his lung pathology. He received intravenous oxygen at the rate of 5.5 cc per minute for 12 minutes and 7.2 cc for 20 minutes, at which time the oxygen was stopped. The arterial blood sample was taken seven minutes later and was 44.9 per cent saturated. Eleven minutes later it was 57.4 per cent. His symptoms started after he had received 5.5 cc of oxygen per minute for 12 minutes and 7.2 cc for three minutes. The symptoms stopped ten minutes after the oxygen was eliminated. They consisted of difficulty in breathing, cough, yawning, feeling of faintness, restlessness, and profuse perspiration. In 15 minutes, these symptoms were followed by clonic contractions of both upper extremities, left facial paralysis, and aphasia. However, he remained conscious. Respirations increased from 20 to 28, and blood pressure from 120/90 to 185/100. The pulse, hemoglobin, and hematocrit all remained constant. There seemed to be some relief of the early symptoms when the patient was placed in Fowler's position.

**Case 3**—This patient was a 36-year-old white man, upon whom a palliative gastroenterostomy had been performed for inoperable carcinoma of the stomach six days previous to this study. Examinations of the heart and lungs were negative. The laboratory findings included a red cell count of 4,000,000, hemoglobin 11.5 Gm, total proteins 6.6 Gm per 100 cc. The oxygen was administered intravenously at a rate of 4 cc per minute for 20 minutes, when the arterial oxygen saturation dropped from 87.7 per cent to 75.3 per cent. The oxygen was stopped at this time because of blood clot formation in the needle.



He then received 6 cc of oxygen per minute for 40 minutes, at which time the arterial blood oxygen saturation was 77 per cent. The rate was then increased to 10 cc per minute. Eight minutes later, he suddenly commenced to cough, perspired very profusely, and was obviously very apprehensive. He also complained of a feeling of compression about his lower chest. The oxygen was stopped six minutes after the onset of symptoms, at this time the arterial oxygen saturation was 64.2 per cent. All symptoms disappeared 20 minutes after the oxygen was stopped. Pulse, blood pressure, hemoglobin, and hematocrit readings were essentially constant throughout this study. Respirations increased from 25 to 30. Anteroposterior and lateral roentgenograms of his chest, taken before and during the administration of the oxygen, failed to reveal any visible gas bubbles or other changes in the heart or lungs. Electrocardiographic tracings were also recorded before the administration of oxygen, again, at the 6 cc per minute rate, and, again, ten minutes after the oxygen flow had been stopped. The following deviations from the control electrocardiogram were noted in the latter two tracings: (1) flattening of the T-waves in the first leads, (2) a distinct elevation of the T-wave above the base line in the third leads, and (3) a diphasic T-wave in the fourth leads.

**Case 4**—This patient was a white male, age 62. Eleven days previous to this study, a calculus had been removed from the common bile duct and a cholecystectomy performed. His postoperative course was uneventful. The red blood cell count was 4,500,000, hemoglobin 12.8 Gm, total protein 7.9 Gm per 100 cc. The electrocardiogram taken prior to surgery and another taken at the onset of the experiment revealed a bradycardia, frequent extrasystoles, and a sinus arrhythmia. The arterial blood oxygen saturation at the onset was 91 per cent. It dropped to 83.5 per cent after he had received oxygen 24 minutes at the rate of 4 cc per minute. The rate of oxygen flow was then increased to 6 cc per minute. Seven minutes later, the patient suddenly complained of precordial pain. He was restless and perspired profusely. The oxygen was stopped immediately at the onset of his symptoms. Eight minutes later, the arterial blood oxygen saturation had fallen to 65.5 per cent. The precordial pain disappeared shortly after he had received 100 per cent oxygen by mask. The pulse increased from 52 to 66, respirations from 20 to 28, and blood pressure from 90/60 to 100/60 during his symptoms. The hematocrit and hemoglobin values remained constant. Electrocardiograms were taken before and during the administration of the oxygen at rates of 4 cc and 6 cc per minute. The following changes were noted in the latter two tracings: (1) flattening of the T-waves in leads I and IV, and (2) elevation of the take-off of the S-T segments in lead IV.

**Case 5**—The first attempt to treat a patient in shock occurred when a 52-year-old colored laborer suddenly lapsed into severe shock 12 days following a subtotal gastric resection for carcinoma of the stomach. His condition was evidently caused by the rupture of a lesser omental cavity abscess, although he had had no fever or other clinical signs indicating its presence. When seen by us, plasma had been started. His blood pressure was 80/60, pulse 144, respirations 38. He complained of severe abdominal pain, and the abdominal findings were those of acute diffuse peritonitis. Under cyclopropane anesthesia, his abdomen was opened. At this time, intravenous oxygen was started. No immediate changes were noted. Surgery consisted of attempts to wall-off the abscess with omentum and in draining it. During surgery, the pulse gradually rose to 180, respirations remained constant, and blood pressure fell to 66/50. Immediately post-operative, the patient rallied somewhat, with a blood pressure of 104/58. During this time he received a 500-cc blood transfusion. He soon, however, lapsed back into his preoperative condition, and progressively declined until his death five hours later. During this last interval, his blood pressure varied from 80/60 to 60/50, his pulse stayed at 155, and respiration at about 52. Except for three short periods of time, intravenous oxygen was given continuously until his death at a rate of 10 cc per minute. No changes were noted in the patient's condition during these periods. Autopsy revealed a perforated jejunal ulcer, with a generalized suppurative peritonitis, moderate pulmonary edema, and approximately 1 cc of gas in the right ventricle and 3-4 cc in the pulmonary artery. The

patient died from the severe toxemia of suppurative peritonitis. In summarizing this case, we feel that the oxygen did not benefit nor, on the other hand, did it appear to be detrimental to him.

**Case 6**—The second attempt to treat a patient in shock was made with a 59-year-old colored laborer with an inoperable carcinoma of the head of the pancreas and a complete obstruction of the common bile duct. He received  $\frac{1}{4}$  grain of morphine sulphate and  $\frac{1}{120}$  grain of atropine sulphate preoperatively. Surgery consisted of palliative cholecysto-enterostomy, and entero-enterostomy. The patient left surgery in a state of moderate shock, with a blood pressure of 86/68, pulse 92, and respiration 26. Intravenous oxygen was started one hour later at a rate of 8 cc per minute, at this time his blood pressure was 89/80, pulse 80, and respiration 28. Five minutes later, the patient became more talkative and seemed somewhat more oriented. The blood pressure rose to 110/80, but the pulse and respiration remained the same. The oxygen was continued for one hour and fifteen minutes, at the end of which time the blood pressure was 110/88, and respiration was 26. In this case, it appears that intravenous oxygen was of benefit to the patient. However, progressive improvement in his postoperative condition was evident before the oxygen was started. During the periods of oxygen administration to both of the last two cases, there was no clinical evidence of pulmonary embolism nor of increased hypoxia. Unfortunately, arterial oxygen determinations were not done in either case.

#### IN VITRO EXPERIMENT

**In Vitro Experiment**—An attempt was made to approximate the amount of absorption of oxygen that occurred in the venous blood during its passage from the intravenous needle to the lungs. Fifty cubic centimeters of venous blood were drawn from a dog with an oiled syringe containing potassium oxalate. The blood was injected under a covering of mineral oil into a 50 cc burette and a sample drawn from the burette for oxygen determination. Three cubic centimeters of oxygen were slowly injected into the bottom of the burette. The burette was held at such a slant that it took approximately ten seconds for each gas bubble to pass through the blood column to the top of the burette. Blood samples were again drawn, and no changes were noted in the oxygen saturation in this blood. It was observed that the oxygen bubbles rose along the upper surface of the blood column, and, thereby, reduced the amount of gaseous surface exposed to the blood for absorption. This same observation had also been made in several dog experiments in which oxygen was injected into the femoral vein and its passage through the inferior vena cava noted. Here, likewise, the gas bubbles had coalesced and rode along the upper surface of the column of blood.

**DISCUSSION**—In experiments on intravenous administration of oxygen to dogs, it had been shown by several investigators that there resulted a fall in the oxygen saturation of the arterial blood. Grodins, Ivy, and others concluded that this hypoxia was due to gaseous pulmonary embolism. In our study of four cases, we, likewise, obtained a consistent fall in the oxygen saturation of arterial blood. This decrease in the oxygen saturation was marked. However, the values are comparable to those obtained in high altitude experiments in which the degree of hypoxemia was correlated with symptoms.<sup>8</sup> We also believe this fall to be due to gaseous pulmonary embolism.

Only a very small part of the gas is absorbed into the blood during the passage of the gas through the systemic veins, heart, and pulmonary arteries. Absorption does not take place because only a very small surface of the gas is exposed to the blood column in the vessels. Moreover, as the oxygen left

the gas bubbles, nitrogen and carbon dioxide would enter the bubble. The pressure of the gases in the bubble is atmospheric, or approximately 760 mm mercury. The pressure of the gases dissolved in the venous blood is 703 mm.<sup>9</sup> Hence, the bubble of gas would disappear at a rate dependable upon the difference between the gas pressures of 760 mm and 703 mm and not upon the difference of pressure between 760 mm and the pressure of oxygen in the blood (approximately 40 mm). That the gas bubble may not completely disappear in the venous blood is evidenced by the autopsy performed on the fifth patient who received oxygen intravenously up to the time of his death. One cubic centimeter was found in the right ventricle and 3-4 cc in the pulmonary artery. The gas had not been absorbed even though it had been in contact with the blood for 25 hours following his death, when the heart was opened under water. Still another factor although minimal, that would diminish the absorption of the oxygen into the venous blood is the higher content of carbon dioxide in this blood as compared to the blood in the pulmonary capillaries.

We feel that oxygen bubbles of fairly large diameter reach and occlude the smaller pulmonary arteries or at least occlude the arterioles. It is unlikely that the pulmonary capillaries are themselves primarily occluded, because if the gas bubbles were small enough to reach the capillaries, their surface exposure would probably be large enough for rapid absorption of the gas by the blood to occur. Moreover, what oxygen was not rapidly absorbed would tend to pass into the alveolar spaces, as the oxygen tension in the gas bubbles would be greater than the 105 mm oxygen tension in the alveoli. Finally, with a comparison of the size of the pulmonary capillary bed to the small amount of oxygen used in these experiments, it appears evident that occlusion of the capillaries alone would be too minimal to cause the changes noted in the experiments.

Three patients exhibited symptoms of pain in the chest, cough, and restlessness, and the first four patients sweated profusely and had a slightly increased respiratory rate. These symptoms, likewise, appear to be due to pulmonary embolism, for they are exactly analogous to those that occur in the "chokes" of nitrogen pulmonary embolism at high altitudes. That the administration of intravenous oxygen does result in arterial hypoxemia is evident by the consistent measured decrease in the arterial oxygen saturation that occurred in the four patients upon whom these determinations were made. This fall in oxygen saturation progressed as more oxygen was given either at a faster rate or for a longer period of time. That a systemic hypoxia occurred may be evident from the following:

- 1 Symptoms of cerebral hypoxia occurred in one patient. They consisted of aphasia, facial paralysis, and clonic contractions of his upper extremities.

- 2 Symptoms of myocardial hypoxia occurred in another patient and consisted of precordial pain.

- 3 Changes in electrocardiographic tracings occurred in the two patients of whom they were taken. These changes were in the T-waves and the S-T

segments and are comparable to those occurring in the anoxic test for angina pectoris<sup>10</sup>

The cause of the arterial hypoxemia is apparently pulmonary occlusion. The reflex vasospasm and possibly bronchospasm resulting from the pulmonary embolism may be a further significant factor in the cause of the hypoxia.<sup>11</sup> That this reflex spasm does occur is suggested by the following

1 The occurrence of vagal stimulation has been shown by the experiments on dogs, in which sectioning of the vagi prevented the shallow rapid respirations that resulted from intravenous oxygen.<sup>7</sup> In our human experiments, vagal stimulation may explain the lack of the increased pulse rate in spite of the presence of hypoxia.

2 That sympathetic stimulation occurs is evidenced by all of the first four patients displaying marked profuse perspiration, and by the fact that the blood pressure either remained constant or became elevated in spite of decreased pulmonary circulation.

3 Cases have been reported in which a small pulmonary embolus produced marked symptoms which were relieved with large doses of atropine and papaverine.

4 Intravenous oxygen was given to one patient for one hour and fifteen minutes at the rate of 8 cc per minute without the development of any pulmonary or hypoxic symptoms. This patient had been atropinized and was in the state of shock. It is possible that these factors prevented some of the reflex spasm.

#### SUMMARY

1 Intravenous oxygen was administered to two patients in shock and to four patients who were not in shock, and were considered to be in relatively stable cardiorespiratory condition. Clinical observations alone were made on the last two patients. Clinical and laboratory studies were done on the first four.

2 One experiment was done *in vitro* to approximate the amount of oxygen absorbed by the venous blood during the passage of the gas bubble from the intravenous needle to the lungs.

3 No definite clinical changes were noted in the first patient who was in shock. There was possible clinical improvement that could be attributed to the oxygen in the second patient in shock. Moreover, there was no clinical evidence of pulmonary embolism nor of systemic hypoxia. In the other four patients there was a marked and consistent decrease in the oxygen saturation of the arterial blood. This decrease was evidenced by actual arterial oxygen saturation determinations, symptoms of systemic hypoxia, and by electrocardiographic changes. Three of these last four patients gave clinical evidence of pulmonary embolism.

4 Studies on the passage of oxygen bubbles through a sample of venous blood at rates comparable to intravenous administration, failed to show any appreciable absorption of the gas by the blood.

## CONCLUSIONS

1 The amount of oxygen absorbed by the venous blood from the time of its introduction into the vein until its passage to the smaller pulmonary arteries is insignificant. The gas bubbles coalesce in the veins. Therefore, they are of considerable diameter upon their arrival at the smaller pulmonary arteries, and occlude these vessels.

2 The resulting gaseous pulmonary embolism causes a decreased pulmonary circulation, arterial hypoxemia, and systemic hypoxia. These effects are probably intensified by reflex pulmonary spasm and possibly also bronchospasm.

3 It is possible that some of the ill effects of pulmonary embolism, and thereby arterial hypoxia, may be alleviated by the administration of atropine and papaverine before intravenous oxygen is given. Likewise, a state of shock or of anesthesia may diminish these reflexes and thereby permit the oxygen to be given.

4 In its present status the value of intravenous oxygen as a therapeutic measure is doubtful. Because of pulmonary embolism it is definitely hazardous.

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# LARYNGO-ESOPHAGECTOMY

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THE MANAGEMENT of advanced cancer of the larynx presents a difficult and often discouraging problem. Not infrequently these cases are seen with their disease so far advanced that surgery and/or radiation offers palliation for a short time only.

That intrinsic cancer of the larynx will remain localized for many months and even years is well recognized. Yet, when it gets beyond the bounds of its cartilaginous cage it will produce regional lymph node or soft-tissue involvement and even distant metastases.<sup>1</sup> Cancer of the extrinsic larynx usually grows much more rapidly. Often cervical lymph node involvement is the first evidence of the disease. Patients with this advanced disease are seldom operable. If given a course of radiation therapy which is lethal for cancer cells necrosis and slough of both cartilage and soft-tissues may occur.<sup>2</sup>

The patient with extensive intralaryngeal necrosis must have a laryngeal fissure to remove the necrotic material and prevent its aspiration into the bronchial tree. Eventually a majority of these patients die either from recurrent disease, sepsis, pneumonia, pain and inanition, or hemorrhage.<sup>3</sup> Brunschwig<sup>4</sup> recently emphasized these points in describing his procedure for panlaryngectomy.

The case being reported had all these complications, and the patient has now been restored to usefulness and apparent good health.

**Case Report**—J. F. M., a 60-year-old white male, was admitted to the Tumor Service, June 10, 1943, with a chief complaint of difficulty in breathing.

**Present Illness** Patient had been in excellent health until approximately one year prior to admission, when he began to notice a dull, aching pain in the left side of his neck radiating upward to his left ear. Shortly after this he noticed some hoarseness in speaking. He consulted his local physician who prescribed local medication and sedation, without relief. His hoarseness became progressively worse. During the month prior to admission he experienced difficulty in breathing and some difficulty in swallowing. He had lost approximately 20 to 30 pounds in weight during the past year. Review of his other symptoms revealed nothing of note.

**Past Medical and Family History** Irrelevant.

**Physical Examination** The patient was a tall, thin, extremely dyspneic white male. There was marked suprasternal retraction with each attempt to inspire. The larynx could not be seen clearly on mirror examination. The entire left larynx was immobile, and there appeared to be a diffuse swelling extending from the base of the epiglottis downward to involve the entire ventricular region, false cord, and partially obscuring the true cord on the left side. No definite ulceration was seen. Crepitation was absent on both sides of the larynx. There was no regional lymph node enlargement. Lungs were clear. Heart was normal size. The rhythm was interrupted by frequent extra systoles. There were no murmurs. Abdomen was flat. Liver was enlarged two finger breadths below the right costal margin. Otherwise physical examination was not remarkable.

*Clinical Course* Because of his extreme difficulty in breathing, an emergency tracheotomy was performed. Three days after admission a biopsy, obtained from the region of the left ventricle, showed squamous cell carcinoma, Grade II. At this time a more satisfactory examination of the larynx was possible. The lesion was found to involve the entire left half of the larynx and posteriorly extended to the right. Because of the extent of the disease and probable extension into the esophagus posteriorly, radiation therapy was believed to be the treatment of choice. Between June 10 and August 31 he received 3,550 r to each of two 6.4-cm circular ports directed to cross-fire the larynx. Factors: 250 kv, 50 cm target skin distance, 1.5 cu filter. Patient tolerated his treatment well. Regression of the tumor appeared to be slow. There was rather marked skin



FIG 1



FIG 2

FIG 1—Patient 24 hours postoperative. Tube for feeding is in upper end of esophagus.

FIG 2—Pedicle grafts developed on chest have been shifted to sternoclavicular area. Necrosis in soft-tissue on right side of neck is where common carotid artery perforated.

reaction. On August 13th tracheotomy tube was removed and the stoma permitted to close. Breathing was normal and without difficulty. He was discharged from the hospital on August 13, 1943.

Patient remained symptom-free until October, 1943, when he again reported to the Clinic complaining of difficulty in breathing, cough and pain in his chest. Roentgenograms and physical findings indicated right lower lobe bronchial pneumonia, temperature 103.4° F, pulse 110, respiration 32. Indirect examination showed the larynx to be very edematous. This edema also involved the subcutaneous tissues of the entire neck. Tracheostomy stoma was reopened and considerable purulent material was expelled from the bronchial tree. It was quite evident that extensive necrosis of the larynx had occurred. A laryngeal fissure was performed and the laryngeal cavity packed with iodoform gauze. The patient was given sulfadiazine to control the pneumonia and local infection. From day to day portions of necrotic soft-tissue and cartilage were removed through the laryngeal fissure. After four weeks the patient was relatively symptom-free other than some pain in the left side of his face and in the left temporal region. This pain was not severe enough to interfere with his employment as a gardener. He was discharged.

He again reported to the Clinic, December 22, 1944, complaining of very severe pain in the left side of his head and left neck. Cervical roentgenologic studies showed residual portions of the laryngeal cartilages. Mirror examination showed some slough and necrosis in the epiglottis. Biopsies obtained from the posterior and lateral walls of the tracheostomy stoma revealed extensive recurrent carcinoma. Because of previous extensive radiation therapy the skin was not thought to be able to withstand additional therapy. The extent of disease made surgical extirpation inadvisable. Interstitial radiation with radon was believed the procedure of choice. In divided doses, 21 gold seeds, totaling 19.46 mc, were inserted into the tumor-bearing area. It was believed this additional radiation would produce further necrosis and slough, as the tumor was destroyed. Eighteen days after implanting the last radon, extensive necrosis of the soft-tissues had occurred. Because of the probability of a fatal hemorrhage, a block dissection was believed advisable. On March 22, 1945, the patient was operated upon, under intravenous sodium pentothal anesthesia, and a resection of the residual larynx, cervical trachea, anterior soft-tissues of the neck, and cervical esophagus was performed.

*Operative Procedure* Under sodium pentothal anesthesia, an incision was made along the anterior border of the right sternomastoid muscle. By careful blunt and sharp dissection the medial strap muscles were divided below and left attached to the residual larynx and hyoid bone. The right carotid sheath was stripped of all fascia. The dissection extended from the clavicle to one-half inch above the hyoid bone. A similar procedure was followed on the left side, thus, the entire larynx was mobilized laterally. Dissection was then carried across the midline in upper portion, cutting through all fascia and muscles above



FIG 3—Diagram showing attachment of tube-pedicles to neck

the hyoid bone. The hyoid bone was divided on either side just anterior to the cornu. The hypopharynx was opened, the mucous membrane of the upper border being clamped prior to cutting to control hemorrhage and prevent retraction. A finger was then inserted through this opening in the hypopharynx into the esophagus. By means of sharp dissection the anterior three-quarters of the cervical esophagus, together with the larynx and trachea was resected from above downwards to approximately one-half inch above the sternum. At this level the trachea and esophagus were amputated. Careful hemostasis was obtained by ligating all bleeding points with No. 000 catgut. The skin was mobilized on either side and sutured with fine black silk over the exposed carotid arteries and internal jugular veins to the small strip of esophageal mucous membrane. The mucous membrane of the anterior hypopharynx was sutured to the skin of the submental region. The trachea was sutured to the skin with interrupted silk sutures. A catheter was then inserted into the esophageal stoma and light dressing applied (Fig. 1). The patient received a transfusion of 500 cc of intrated blood on the operating table. The operation was well-borne.

*Postoperative Course* Patient's postoperative course was complicated by separation of the suture line on both sides, and considerable secondary infection on the right. Healing by secondary intention on the left side was slow, but satisfactory. On the right, the wide separation of the wound edges was followed by some necrosis.

On April 26 and July 12 tube-pedicle grafts were prepared on either side of the chest (Fig. 2). These were to be used to reconstruct the cervical esophagus. On July 22



(three months after his block resection), the right common carotid artery perforated. Fortunately, one member of the Staff was on the floor at the time and immediately ligated this vessel. Ligation was followed by a convulsive seizure which lasted approximately 30 seconds. The patient remained somewhat stuporous for approximately three days. No permanent sequelae resulted from the ligation of this vessel.

By successive steps the tube-pedicles were advanced from chest to the base of the neck on either side of the esophageal stoma, and then advanced to the submental region (Fig 3). After circulation had been well-established in this area, secondary infection had subsided and wound healing completed, the tube-pedicles were sutured to the neck. An



FIG 4

5-11-71  
W 94 TO AD



FIG 5

FIG 4—Continuity of esophagus has been established. Patient is able to eat a regular diet.

FIG 5—Radiograph with barium swallowing shows some puddling in lower portion of artificial esophagus and slight constriction at line of anastomosis.

incision was made on the posterior border of each tube. A corresponding incision was made in the skin on either side of the neck and adjacent surfaces were sutured with interrupted fine black silk. Healing of these anastomoses was prompt and complete. On January 17, 1946 the clavicular portions of the tube-pedicle grafts were freed on either side and brought across the midline. The muscle and mucous membrane of the esophageal stoma was opened and the cut-end of the pedicle sutured to the upper end of the esophagus. Healing of this anastomosis was satisfactory. On March 14 an incision was made along the adjacent surfaces of the tube-pedicles. The tubes were opened, the skin was undermined and corresponding edges approximated. The inner surfaces were sutured with interrupted mattress sutures of plain No 0 catgut to form the lining of the reconstructed cervical esophagus. The external surfaces were approximated with interrupted sutures of fine black silk. The healing of the two grafts was rather slow and complicated by slight superficial infection in the midportion, which subsided under penicillin therapy. On the 5th postoperative day the patient was taking liquids, and on the 20th postoperative

day he was able to swallow a regular diet (Figs 4 & 5) Patient is now employed as a farm laborer. He has gained 37 pounds in weight and appears to be free of disease.

COMMENT: Resection of the cervical esophagus and larynx for cancer of the cervical esophagus is an accepted procedure. Block resection of the structures of the neck bounded by the carotid arteries laterally and the cervical vertebrae posteriorly is a more extensive procedure. It is justified when one considers the hopelessness of the condition being treated. Its use must be limited to patients in whom no wide extension or distant metastasis can be demonstrated. During the past year three other patients with similar stages of disease as the patient reported in this paper were seen in the clinic. One refused further surgery after his left common carotid artery had been ligated to control hemorrhage. The second case had a fatal hemorrhage the week before this operative procedure was to be performed. At autopsy, the disease in both was found to be localized to the neck and grossly would have been entirely included within the operative field. The third case has recently been resected. Reconstruction of the removed portion of his esophagus will be performed.

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# LEIOMYOMA OF THE KIDNEY

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THE DISCOVERY of a large retroperitoneal mass in infancy and childhood leads one immediately to a consideration of the two most common lesions in that age-group, namely, neuroblastoma and Wilms' embryoma of the kidney. The literature of surgery, pediatrics, urology and pathology is replete with case reports and discussions of these interesting conditions<sup>5, 6, 7</sup>. Occasionally, however, the surgeon is surprised to find a benign tumor in a case in which the preoperative diagnosis was that of malignancy, as in the case of a leiomyoma of the kidney in a newborn child, the subject of this paper. In an examination of such standard texts as Ladd and Gross,<sup>1</sup> Campbell,<sup>2</sup> and Brennemann,<sup>3</sup> the reader will find no mention of leiomyoma of the kidney and Ewing<sup>4</sup> dismisses the subject with the statement that "in the kidney, small myomata and myolipomas occur in capsule or cortex and appear to be derived from fragments of capsule tissue."

Leiomyomata of the kidney in older age-groups have been reported on rare occasions from time to time, and, in general, may be said to consist of three types

- 1 Small, frequently multiple myomata, several millimeters in diameter, found beneath the kidney capsule or in the superficial cortex. They are encountered as purely accidental findings at autopsy in individuals who have died from other causes.

- 2 Large solitary growths causing symptoms and discovered during the life of the individual.

- 3 Myomata which appear to be malignant or have undergone definite sarcomatous changes.

Cases of the first variety have been reported by Busse,<sup>11</sup> Lartigau and Larkin,<sup>13</sup> Hess,<sup>15</sup> Hallas,<sup>16</sup> and Krietschmer.<sup>20</sup> The first recorded case of the second category was that of a large myoma of the renal hilus reported by Schluter,<sup>8</sup> in 1890. Four years later, Regnier<sup>9</sup> presented a myoma of the renal capsule, and Reverdin<sup>10</sup> described a 48-pound fibromyoma of the fatty capsule of the kidney. In 1899, Busse reported a large fibromyoma, and Ochsner<sup>12</sup> demonstrated a case of leiomyofibroma of the kidney weighing 4,600 Gm, and consisting mostly of fibrous tissue. In 1914, Hoffman<sup>17</sup> reported a case of leiomyoma of the kidney in a woman, age 35, and 14 years later, Bugbee<sup>18</sup> described a leiomyoma of the kidney in a woman, age 35. The tumor was 13.5 cm in its longest diameter, appeared beneath the renal capsule and was sharply circumscribed and enveloped in a thin fibrous capsule. Crosbie and Pinkerton,<sup>21</sup> in 1932, reported a large, encapsulated lobulated leiomyoma

in a woman, age 35. The tumor seemed to arise from the outer wall of the pelvis but eventually became imbedded in the kidney substance. In 1935, Heggie and Alstead<sup>25</sup> described a tumor 6.5 x 5.5 x 3.75 inches in a woman, age 40. It was well-encapsulated and the blood vessels, present in moderate amount, were well-formed. The authors surmised that it might have arisen from a small tumor beneath the capsule, but in its advanced growth, the origin could not be stated definitely. Counseller and Menville,<sup>30, 31</sup> in 1936, described a case in a woman, age 29. The tumor was associated with benign cysts in a kidney with duplicate pelvis. In 1937, Michon<sup>28</sup> added a case of angiofibroleiomyoma, and Marion<sup>27</sup> a case of angioleiomyoma. In their report, Bailey and Harrison<sup>32</sup> included a leiomyoma weighing 4,940 Gm. and measuring 38 x 24 x 11 cm. This tumor occurred in a woman, age 26. In 1939, Gordon, Kimmelsiel and Cabell<sup>33</sup> described the youngest case yet on record, a girl age 15, in which the tumor was like a myoma of the uterus. The last recorded case was that of Ciabtree,<sup>34</sup> in 1944, who described a leiomyoma of the kidney with cystic degeneration and calcification in a male, age 39.

Several malignant muscle tumors of the kidney have been reported. Jacobaeus,<sup>14</sup> in 1903, described multiple angiosarcomas of the kidney in a case of tuberous sclerosis, and Hallas,<sup>16</sup> in 1912, recorded a fibromyo-endothelioma that had metastasized to the aortic lymph nodes, in the capsule of a woman, age 59. Berry,<sup>19</sup> in 1929, reported a leiomyosarcoma of the kidney in a woman, age 26, which had a well-defined capsule in some places and not in others, and which, on microscopy, showed the capsule to be split in places. In 1933, Cooke<sup>22</sup> reported a malignant leiomyoma which had replaced the right kidney in a woman, age 60, and Swan<sup>23</sup> described a leiomyosarcoma of the left kidney removed from a male, age 71. In his series of tumors, Smith<sup>24</sup> included one case of leiomyosarcoma of the kidney. In 1937, Mintz<sup>26</sup> contributed two cases of leiomyosarcoma, and Patch<sup>29</sup> a case of malignant leiomyoma.

The case we are presenting is unique even in so rare a tumor as leiomyoma of the kidney. It is the first recorded case of a large solitary leiomyoma of the kidney in a newborn child.

**Case Report**—Baby S was born on July 17, 1946 at the Beth El Hospital, a full-term, white male infant, delivered by low forceps application. The delivery was uneventful and the baby began to breathe spontaneously. His birth weight was six pounds and six ounces, and his length 20.5 inches. He was the third child born of this mother, the other two children being normal in every respect. There was no history of neoplasia in the family.

Immediately after delivery, it was noted that the baby's abdomen was somewhat enlarged, and examination revealed the presence of a large abdominal tumor. The patient was transferred from the nursery to the Pediatric Service for further study.

Examination showed a full-term, alert, vigorous male infant, who was somewhat pale. Temperature 98° F. The baby was normal in all respects except for the abdominal mass. The abdomen was soft, and no fluid was detected. The mass filled the left side of the abdomen, extending from the left costal margin to the left iliac crest and from the midline to the left loin. The tips of the fingers could just be placed beneath the left lower ribs and the upper margin of the mass. The surface of the tumor was perfectly smooth and its consistency firm. There was apparently no tenderness on palpation and the mass

was mobile, as could be demonstrated by pushing it forward from the loin. Its anterior border in the midline was round and smooth, but the posterior border could not be detected. The liver and spleen were not palpable, nor was the kidney on the right side. Micturition and defecation were normal and urinalysis revealed no abnormalities. The blood count was R B C 5,790,000, Hb 119 per cent (18.3 Gm), W B C 9,600. No erythroblasts or pathologic cells were found on blood smear. The blood sugar was 82 mg per cent, and the blood urea was 9.4 mg per cent. An intravenous pyelogram, using six cubic centimeters of diodrast, was done. Roentgenograms revealed the presence of a large mass in the left abdomen (Fig. 1) which displaced the intestines and colon upward and to the right. The right kidney was normally visualized. The pyelographic outline on the right side appeared normal. The left kidney outline was not identifiable. A speck of contrast medium appeared in the region of the left kidney pelvis, and the kidney appeared to be displaced upward and to the right. The impression was that of the presence of a left kidney neoplasm.



FIG. 1—Pyelogram of kidneys. Note displacement of left colon. Arrow indicates contrast medium in left pelvis.

The child did well on an evaporated milk formula and, July 29, 1946, operation was performed (I C Z). Under drop-ether anesthesia, the abdomen was opened through a left upper rectus muscle-splitting incision extending slightly below the umbilicus. On entering the peritoneal cavity, a large retroperitoneal mass on the left side presented itself. This mass pushed the left colon toward the midline and the spleen upward. The liver was grossly normal. The right kidney was palpated and found to be normal, but the left kidney could not be identified. The mass was the size and shape of a baseball, smooth and very firm. The left lateral peritoneum was incised and the retroperitoneum entered. The tumor was found to be well-circumscribed and was easily shelled out except medially where a pedicle was encountered. This pedicle consisted of the ureter and renal vessels which were not invaded by the tumor mass. They were ligated individually, following which the tumor was easily removed. The nephric

space was packed with thrombin-fibrin foam because of a slight generalized ooze. The lateral peritoneum was sutured and the abdomen closed in layers, without drainage.

Immediately following the operation, the infant was given a blood transfusion and fluids by scalp vein. Postoperative recovery was complete in 24 hours. The baby ran an unexplained low-grade fever for two weeks, but he ate well and was alert and normal in all his reactions. He was discharged, August 24, 1946, weighing seven pounds and eight ounces, and in good condition. Recent examination of the child has shown that he is progressing well.

*Pathologic Report—Gross.* The specimen consists of an ovoid firm mass measuring 7.5 x 5 cm, to one pole of which is attached a small infantile kidney which measures 3.5 cm in its greatest diameter. The mass is encapsulated by a thin, delicate fibrous capsule.

## LEIOMYOMA OF KIDNEY

It blends imperceptibly with the renal tissue near the hilus but otherwise appears to be fairly well demarcated from the kidney. The mass is uniformly firm throughout (Figs 2, 3 and 4). On section, the cut-surface (which had been previously fixed in formalin) presents the so-called classical watered silk appearance of a uterine myoma. Small vascular spaces are identified in many portions of the tumor. There is no hemorrhage or necrosis. The renal tissue present in the specimen does not appear grossly abnormal.

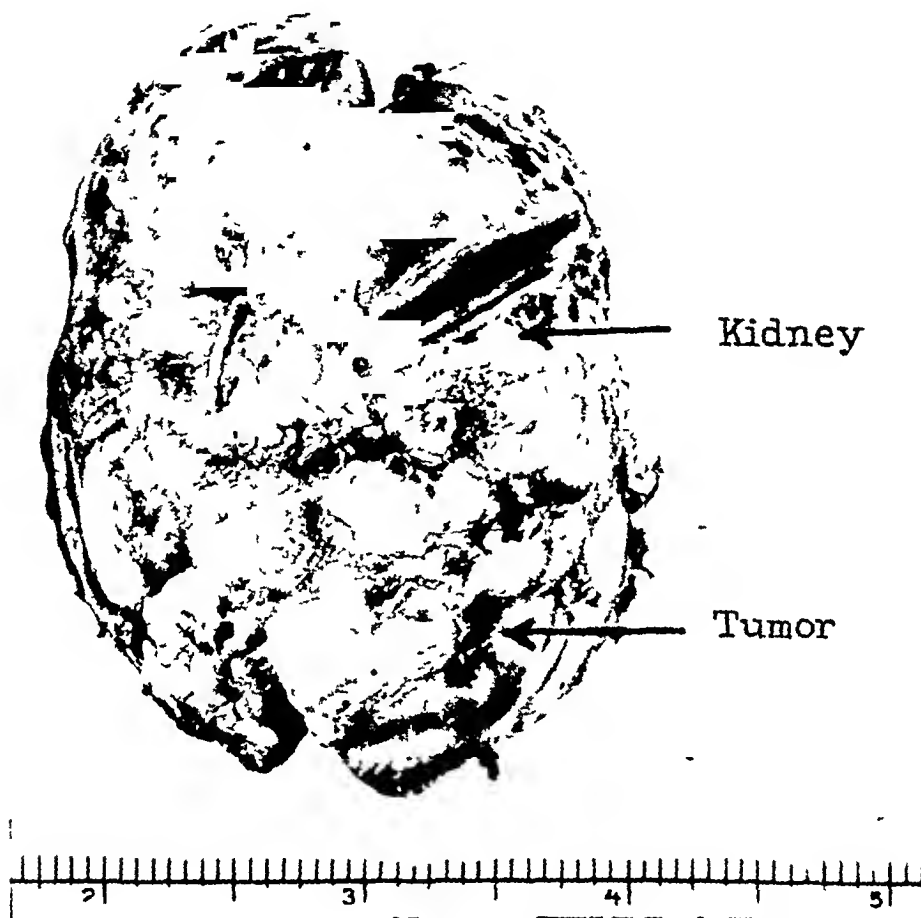


FIG 2—Gross appearance of unopened specimen

*Microscopic* A fairly-well demarcated but encapsulated tumor is present. At the periphery of the tumor small bands of neoplastic tissue infiltrate among the cortical tubules and glomeruli with extension to the subcapsular region. In one section the renal pelvic epithelium is well preserved. The tumor tissue is composed of compact bundles of elongated cells containing vesicular ovoid nuclei which show a tendency to clubbing at their extremities. No mitotic figures are observed. Abundant fibrillar intercellular material is present. The bundles of tumor tissue show a fasciculated appearance. Prominent throughout the tumor are small vascular spaces lined by flattened endothelial cells and containing a few erythrocytes (Figs 5, 6 and 7). *Pathologic Diagnosis* Cellular leiomyoma of the kidney.

*DISCUSSION*—As previously mentioned, leiomyomata of the kidney may be either of the small, multiple, symptomless variety discovered as incidental findings at autopsy or large solitary tumors recognizable during the life of the individual and productive of symptoms. The histogenesis of these tumors is

FIG 3

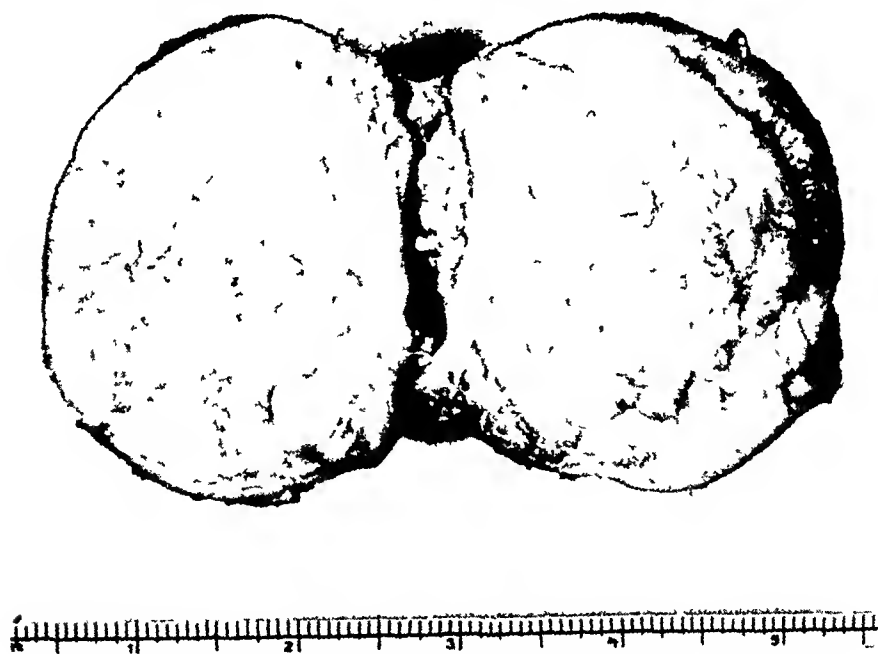


FIG 4

FIG 3—Gross appearance of opened specimen

FIG 4—Gross appearance of tumor Note watered silk appearance of myoma

of considerable interest. Smooth muscle fibers can be found normally in the capsule of the kidney, the kidney pelvis and calices, and the renal vasculature

FIG 5

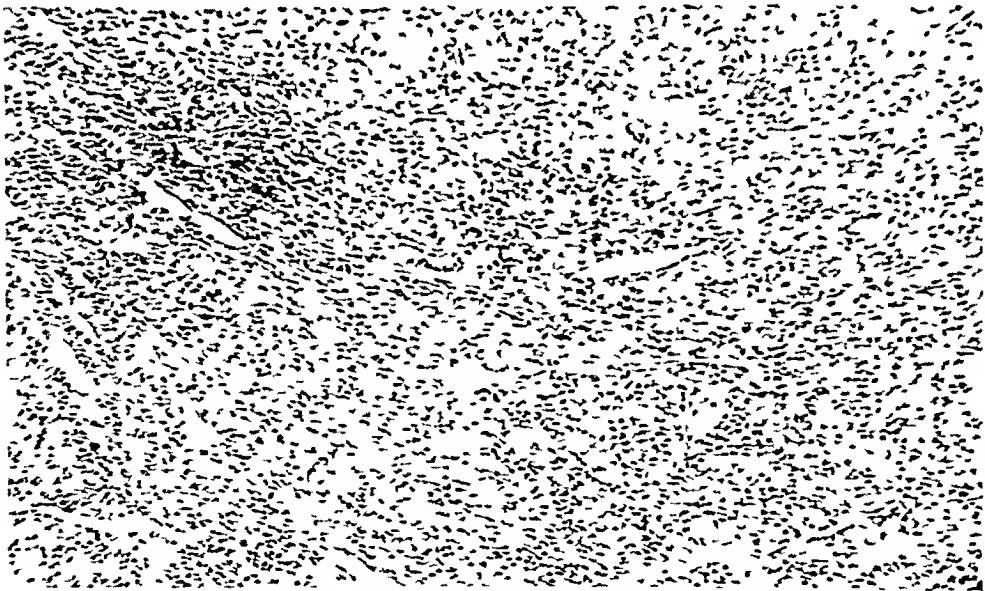


FIG 6

FIG 5—Low power microscopic appearance of tumor. Note epithelium of kidney pelvis.

FIG 6—Low power microscopic appearance of tumor. Note vascular spaces.

They are not found in the parenchyma of the kidney. Busse<sup>11</sup> has described abundant muscle fibers in the medulla of the embryonic kidney. This he claimed



to be a possible source of fibromyomas of the kidney. This observation has not been confirmed by others, and smooth muscle fibers have not been seen outside of the walls of blood vessels in the medulla of the embryonic and fetal kidney (Gordon)<sup>33</sup>. The discovery of small myomata of the cortex in those cases in which the tumor does not appear to be in continuity with the renal capsule can be explained as being choristomas or hamartomas. In the case described by Gordon, *et al*,<sup>33</sup> the outstanding microscopic feature of the tumor was the presence of numerous large blood vessels, giving one the impression that the

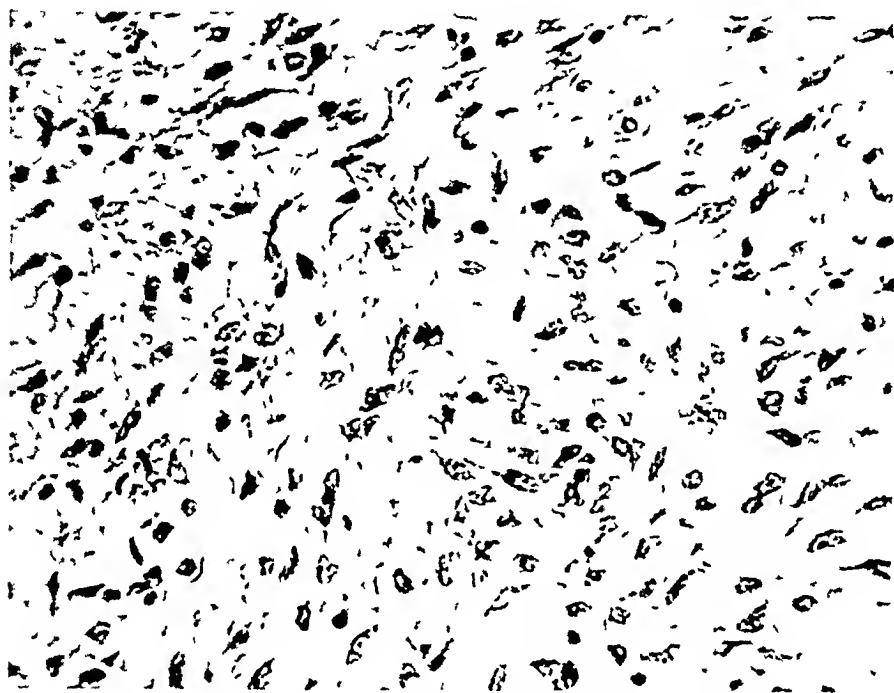


FIG 7—High power microscopic appearance of tumor

tumor was derived from the muscular coats of these vessels, the young muscle fibers arising from the outer and middle coats of the arterial walls. In view of the fact that the main characteristic of the tumor was the formation of large muscular arteries, the authors believed that the proper description for this case was arterioleiomyoma of the kidney.

Some writers (Busse, Hallas, Heggie and Alstead, Hess, Hoffman, Lartigau and Larkin, Michon, Regnier and Reverdin) have expressed the opinion that these tumors arose from the renal capsule, while others (Bailey and Harrison, Counseller and Menville, Crosbie and Pinkerton, and Mintz) believe the origin to be from the renal pelvis or calices. Rubaschow,<sup>35</sup> describing similar lesions of the epididymis, ventured the opinion that they might arise from embryonic rests of the primitive myotome. Oberndorfer,<sup>36</sup> discussing similar lesions in the epididymis, was convinced that a chronic inflammatory process was the most important etiologic factor. There is little evidence, however, to support this view.

Unfortunately, in most cases of large solitary tumors, the advanced growth of the mass precludes any attempt to ascertain its exact origin. In the case here reported, origin from the capsule can be ruled out by the gross relationship of the tumor to the remaining renal tissue. The inclusion of well-defined small vasculature spaces in many sections of the neoplasm suggests derivation from vasculature smooth muscle. However, no definite transition from discrete blood vessel wall to neoplastic muscle could be identified, so that a definite statement concerning histogenesis is impossible.

Clinically, leiomyomata of the kidney present several interesting features. In view of the paucity of reported cases of large myomata of the kidney, generalizations are out of the question. The tumors have previously been found in an age-group varying from 15-71 years, and by far the greater number have been found in women. Both kidneys have been found to be equally involved. The conclusion of Crabtree<sup>34</sup> that leiomyomata of the kidney have a tendency to be associated with renal cysts is not borne out by a review of the literature. Grossly, these tumors have the consistency of hard rubber and on section, present a smooth, white glistening appearance. They are usually well-circumscribed and enclosed in a fibrous capsule. They are of slow growth and present few signs other than a mass and occasionally pain or discomfort. Hematuria is rarely seen, and dysuria and frequency are occasional complaints. Fever, when it occurs, is usually the result of infection of the urinary tract or gross degeneration of the tumor. If sufficiently large so that the calices or pelvis are encroached upon, the pyelogram is of diagnostic value, but, even then, there is no means of distinguishing it from other renal tumors. In the absence of malignant changes, the prognosis of leiomyomata of the kidney following nephrectomy is good, and if malignant change does occur, there seems to be little tendency to invade surrounding tissues.<sup>31</sup> The procedure of choice in the treatment of this condition is nephrectomy.

#### SUMMARY

- 1 The literature of leiomyoma of the kidney is reviewed
- 2 A case of large solitary leiomyoma of the kidney in a newborn child is reported
- 3 The histogenesis of the condition is discussed
- 4 The clinical aspects of the lesion are presented

The authors wish to express their thanks to Dr Nathan Mitchell, pathologist of the Beth El Hospital, for his intensive study of the surgical specimen.

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# CONGENITAL ABSENCE OF GALLBLADDER

## REPORT OF THREE CASES

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IT IS QUITE STRIKING that congenital absence of the gallbladder without other anomalies of the biliary system should be so rare, whereas other anomalies of the biliary system are present in 10 per cent of autopsy cases.<sup>1</sup> Couvoisier<sup>2</sup> collected 25 such cases in 1890. In 1928, Bower<sup>3</sup> reviewed the literature and found 31 cases, the earliest of these cases having been reported by Bergman in 1701. Gross,<sup>4</sup> in 1938, published 38 cases. In 1945, Dixon and Lichtman<sup>5</sup> reviewed 50 cases since 1900, and reported ten additional cases. Our review of the available literature revealed 71 such cases. To this number we wish to add three case reports.

The incidence of congenital absence of the gallbladder is about 0.065 per cent, as calculated from 18,350 autopsies by Talmadge.<sup>6</sup> Kirshbaum<sup>7</sup> reported the incidence of such anomaly to be about one case in 3,661 (0.03 per cent), while Smith, Hall, Mentzer, and Nagel found six cases (0.075 per cent) in 7,919 autopsy specimens.

Syphilis, catarrhal inflammation of the biliary tract, fetal peritonitis, maternal toxins, and mechanical factors all have been advanced by various authors as theories of origin of this anomaly. A more easily defended theory involves the embryology of the biliary tree. The embryologic origin of the biliary tract is intimately associated with that of the liver. The entire biliary system, including the liver, arises as a ventral outgrowth from the gut endoderm in the region of the anterior intestinal portal.<sup>8</sup> From the floor of the future duodenum arises the hepatic diverticulum, a cranial portion which is the anlagen of the bile ducts, and a caudal portion which is to become the gallbladder and cystic duct. Though the hepatic diverticulum is originally tubular, the biliary passage tends to become solid, and it is not until the seventh week that a lumen has been reestablished throughout most of its length. Thus, failure of the gallbladder anlagen to form, or, as Gross<sup>4</sup> suggests, failure of the solid anlagen to become tubular, would result in an absent gallbladder. Miller<sup>9</sup> presents strong evidence that the lumen may sometimes fail to form, as he demonstrated tubular tissue in the hepatoduodenal ligament.

In our review of the literature we found many case reports to be incomplete and a few were available to us only in abstract form. An analysis of the data with respect to age and sex, symptoms, preoperative diagnosis, whether found at operation or autopsy, and attempts to prove an intrahepatic gall-

bladder was made. This material was obtained from a total of 71 cases, 34 of which were reported from surgical procedures while 38 were autopsy reports—one case appearing in both series.

The average age of all cases reported was 46 years at the time of discovery. Females were twice as frequent as males in the entire series. These figures agree with those of Melville<sup>10</sup>. However, when viewed as to autopsy or operative reports, the ratio in autopsied specimens is one to one, while those operated upon have a three and three-tenths to one ratio. This would tend to show that occurrence of the anomaly has little relation to sex, but that symptoms provoking exploration of the biliary tree in this entity follow the same sex ratio as does all surgical biliary disease.

Of the 71 cases 34 gave histories indicating biliary tract disease. Due to the brevity and incompleteness of the earlier reports, this analysis is not necessarily valid.

Of the 34 cases (Table I) operated upon, the preoperative diagnosis in 13 cases was cholecystitis, in eight it was obstruction of the common bile duct, five cases were listed only as exploratory celiotomies, four were found incidental to operations for nonassociated intra-abdominal pathology, and in four cases a preoperative diagnosis was not recorded.

In the series upon whom operations were performed, the gallbladder was reported as absent in all 34 cases, while the cystic duct was reported absent only 15 times. Twenty-one reports noted the condition of the common duct, it being dilated 11 times, containing stones in 11 and appearing normal in seven. The liver was described 13 times. In three cases it was atrophic, in two, hypertrophic, and in two reports anomalies were cited—one being a large Riedel lobe and the other a complete absence of the left lobe.

In the series where the gallbladder was found to be congenitally absent at postmortem examination (Table II), the cystic duct was recorded as absent in 18 cases, the common duct as dilated in four cases, containing stones in only one case, and as normal in seven instances. Ten cases exhibited a pathologic liver, seven of the atrophic variety, and three of the hypertrophic type. Four reports noted anomalies of the liver. In two the quadrate lobe was indistinct, while in a third case the quadrate lobe was absent. The remaining case exhibited nonseparation of the liver lobes.

Visualization of the gallbladder by cholecystograms was attempted in 12 instances. In several patients the attempt was repeated using different methods of administration of the dye. All failed to be visualized.

In one autopsy specimen (Mackmull<sup>11</sup>—1930) and two postoperative patients (Drenckhahn and Rogers<sup>12</sup>—1943, and Dixon and Lichtman<sup>5</sup>—1945), the biliary trees were injected, *via* the common duct, with radiopaque material in an attempt to visualize an intrahepatic gallbladder if present. All failed to reveal a shadow which could be interpreted as a gallbladder.

#### CASE REPORTS

**Case 1**—Mrs. R. A., a 52-year-old white female, was admitted to Wesley Memorial Hospital, September 13, 1945, because of severe cramping pain in the epigastrium, nausea,



**Expenditures**

[illegible]

TABLE I—Continued  
SYNOPSIS OF CASES OPERATED UPON

Author	Age and Sex	Symptoms and Duration Of	Preoperative Diagnosis	Why Operated	Findings at Surgery		Proven Not Intrahepatic-
					No gallbladder or common duct cirrhotic	Liver	
Naegeli	1921	65 F Gallstone colic Vomiting Icterus	30 yrs		No gallbladder Stone in common duct	No	No
		34 F Vomiting, jaundice, acholic stools Pain in R U Q	5 yrs		Com duct dilated	No	No
Niemach	1908	60 F Nausea, vomiting chills fever Abd pain Acholic stools	2 wks	Biliary disease	Gallbladder absent	Stone in common duct	No
Robertson, Robertson, & Bower	1940	45 M Postcibal distress Jaundice and acholic stools	2 yrs	Cholecystitis and com duct obst	Gallbladder and cystic duct not identified Dense adhesions about gallbladder area		Yes at autopsy
		41 F Abd pain and vomiting	3 mos	Cholecystitis	Gallbladder absent	Liver small, with dense adhesions	No Neg X-ray
Sarma	1941	47 F Typical gallbladder symptoms, with calculi		Cholecystitis, with calculi	Absent gallbladder and cystic duct Com duct dilated, with stones		No Neg X-ray
Schmidt	1928	30 F Pain in epigastrium	6 yrs	Cholelithiasis with pericholecystitis	Gallbladder and cystic duct absent Common duct normal		No
Schulz	1914	64 F			Absent gallbladder and cystic duct Com duct dilated, with stones		No
Stone	1908	54 F Jaundice and epigastric pain	5 yrs	Cholelithiasis	Gallbladder absent Hepatic and com ducts dilated, with stones		No
Torrence	1920	38 M Digestion poor, with constipation Chronic appendicitis symptoms	3 yrs	Appendicitis	Absent gallbladder and cystic duct		No
Whipple	1921	52 F Nausea, vomiting, jaundice, pruritis Bloating and belching postcibal gastric pain	2 yrs	Obst of com duct	Gallbladder and cystic duct absent Com duct markedly dilated with stones Pancreatic lymphangitis		No



vomiting, jaundice, and clay-colored stools. The pain had been present for one week, radiating through to the back and up to the right shoulder. It was not related to meals nor foods and was relieved only temporarily by hypodermic injections of opiates. Nausea and vomiting were persistent. Jaundice appeared three days after the onset of pain. She had noted clay-colored stools for two days prior to entry into the hospital. Similar episodes, though less severe, had occurred once ten years ago and again one month prior to her hospital admission.

Physical examination revealed a well-nourished white female appearing moderately ill and having a marked icteric tint to her skin and sclerae. The heart was not enlarged but there were frequent extrasystoles and a systolic murmur was present at the apex. Pulse 68, blood pressure 104/65. Examination of the abdomen revealed no scars, rigidity or masses. Tenderness on deep palpation in both upper quadrants was present.

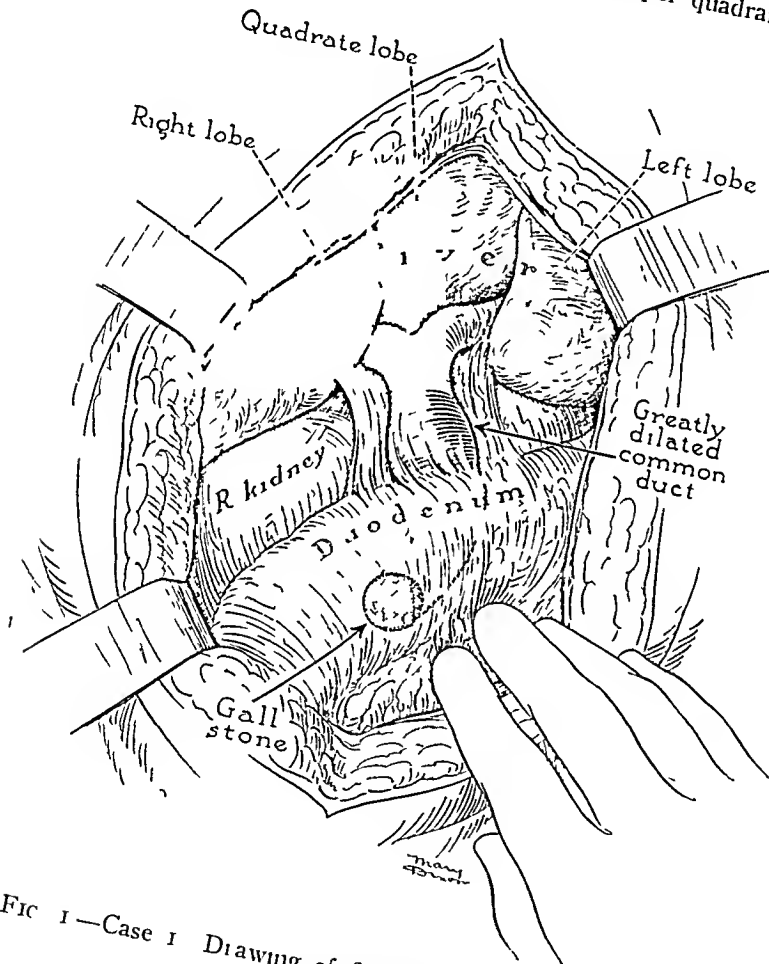


FIG 1—Case 1 Drawing of findings at time of operation

The erythrocyte count was 5,790,000 cells per cm, the hemoglobin 15 Gm per 100 cc of blood, and the white cell count was 5,800 cells per cm. Urinary urobilinogen was absent, while bile was present in the urine, otherwise the urine was normal. The icteric index was 1235 units, and the van den Bergh test revealed a prompt direct reaction with a 9.45 mg per cent quantitative indirect reaction. The stools were clay-colored and contained no bile. The blood proteins on admission were 6.80 Gm of total protein per 100 cc, with 3.87 Gm albumin fraction and 2.93 Gm globulin fraction. An intravenous

TABLE II  
SYNOPSIS OF CASES AUTOPSED

Author	Age and Sex	Symptoms Presented	Autopsy Findings	Proven Intrahepatic	Remarks
Amisat	1831 24 yrs F	Abdominal chest disease	Gallbladder absent, cystic duct present Pancreas enlarged	Autopsy only	
Baker	1835 Nm	Suppurative process	Gallbladder absent, cystic duct not mentioned	Autopsy only	Additional information about symptoms not given
Bergman	1701 Nm	Not mentioned	Gallbladder absent, numerous small cystic ducts Liver showed two lobes not separated	Autopsy only	
Bergman	1836 60 yrs F	Mental disease	Liver enlarged Gallbladder replaced by small fibrous mass	Autopsy only	This case is questionable as gallbladder may have been pre-existent
Buhenhoefer	1905 66 yrs M	Cardiac failure	Gallbladder and cystic duct absent Liver small and cirrhotic	Autopsy only	
Canton	1847 65 yrs F	Cerebral hemorrhage	Gallbladder and cystic duct absent Liver two thirds normal size Common duct twice normal size	Autopsy only	
Danzis	1935 53 yrs F	Belching with vomiting postcibal Pain R U Q radiating to back	No evidence of gallbladder duct found Common duct dissected back into hepatics and live-	Autopsy only	Death following operation
Droste	1853 74 yrs F	Pulmonary disease	Gallbladder absent Cystic duct not mentioned Liver atrophic	Autopsy only	
Eiben	1910 48 yrs M	Pneumonia	Gallbladder and cystic duct absent Common duct not dilated Normal liver	Autopsy only	
Eiben	1910 20 yrs F	Tuberculosis	Gallbladder and cystic duct absent	Autopsy only	
Elvert	1780 Nm	Not mentioned	Gallbladder absent Cystic duct not mentioned	Autopsy only	

Author	Age and Sex	Symptoms Presented	Autopsy Findings	Proven Intrahepatic Autopsy only	Remarks
Eschner	1894 2 yrs	Pulmonary signs and symptoms of rickets	No biliary disease		
Gaultier	1829 60 yrs M	Pulmonary tuberculosis			
Gordon & Dragutsky	1942 76 yrs M	Urinary complaints Anorexia with constipation			
Harle	1856 50 yrs F	Not mentioned			
Hoffman & Jackson	1910 65 yrs F	Pneumonia			
Kehr	Adult M	Not mentioned			
Latham	1897 49 yrs M	Pulmonary tuberculosis			
Lenan	1853 74 yrs F	Pulmonary disease			
Lockhart	1927 24 yrs F	Symptoms of lung abscess			
Loreta	1888 40 yrs F	Not mentioned			
Knov	1922 1 yr F	Bronchopneumonia			
Mackmull	1930 57 yrs M	Pulmonary tuberculosis Constipation with attacks of nausea			
Miller	1936 84 yrs M	No gastro intestinal or biliary complaint Myocardial failure			
Montault	1829 Adult M	Carcinoma of pylorus			

TABLE II—Continued  
SYNOPSIS OF CASES AUTOPSIED  
Autopsy Findings  
Gallbladder absent

No gallbladder	Cystic duct entered liver				
Gallbladder absent	No cystic duct	Com-			
mon duct one cm in diameter					
No gallbladder or cystic duct found					
No gallbladder or cystic duct found	Com				
mon duct dilated					
Absent gallbladder usually large	Cystic duct un				
Gallbladder absent					
Gallbladder and cystic duct absent					
Only pouch of common duct at level of gallbladder site					
No gallbladder or cystic duct found					
Absent gallbladder					
Gallbladder and cystic duct absent					
Absent gallbladder duct in fibrous tissue liver indistinct	Small, blind cystic				
Absent gallbladder and cystic duct atrophic	Quadrant lobe of				
	Liver				

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Cystic duct present and enlarged

Outpouching of common duct present

Retrograde examination of the biliary tree with X ray carried out in cadaver

Remnant of cystic duct present

Autopsy only

Autopsy only

Autopsy only

Autopsy only

Autopsy only

Autopsy only

Autopsy only

TABLE II—Continued

SYNOPSIS OF CASES AUTOPSED						
Author	Age and Sex	Symptoms Presented	Autopsy Findings	Proven Intrahepatic Autopsy only	Remarks	
Möller	1920 28 yrs F	Bronchopneumonia	Absent gallbladder and cystic duct Common duct normal	Autopsy only	Operated for removal of common duct obstruction	
Patterson	1864 35 yrs M	Asthma death	No gallbladder or cystic duct present Liver hypertrophic	Autopsy only		
Robertson & Robertson & Bower	1910 45 yrs M	Indigestion, with postprandial burning Jaundice and clay-colored stools	No gallbladder or cystic duct located Common duct dilated Cirrhosis of hypertrophic type Carcinoma of common duct	Autopsy only		
Sands	1865 29 yrs M	Pulmonary tuberculosis	Absent gallbladder Liver atrophic Absent quadrate lobe of liver	Autopsy only		
Schröner	1916 2 yrs	Not mentioned	Absent gallbladder Syphilis of liver	Autopsy only		
Tunbult & Schröner	1882 Nm	Paretic dementia symptoms	Gallbladder absent Liver small	Autopsy only		
Talmadge	1938 51 yrs M	None	Gallbladder absent Small cystic duct present Hepatic and common ducts dilated Liver normal but quadrate lobe poorly developed	Careful dissection of liver and biliary system		
Trimble	1850 55 yrs F	Infectious disease, with jaundice	No gallbladder or cystic duct Liver atrophic Pancreas contained stone	Autopsy only		
Vergne	1826 26 yrs M	Accidental death	Absent gallbladder and cystic duct	Autopsy only		
Konjetzny	1913 61 yrs F	Attacks of gallstone colic Died from perforation	Absent gallbladder Stone in common duct	Autopsy only		
Dixon	1945 74 yrs M	Epigastric distress Diabetes Hemochromatosis	Gallbladder absent Common duct normal Liver normal	Autopsy only		
Dixon	1945 38 yrs M	Generalized milary tuberculosis	Gallbladder and cystic duct absent Liver normal Common duct normal	Autopsy only		

liver function test revealed only 0.3241 Gm of hippuric acid recovered, compared to 0.5 Gm, or more, for the normal. This figure indicates considerable liver damage—a conclusion supported by gross examination of the liver at operation. The electrocardiogram, taken September 14th, showed changes interpreted as minimal evidence of myocardial damage. A plain film of the abdomen revealed no evidence of opaque biliary calculi. The right diaphragm was elevated. An upper gastro-intestinal tract roentgenologic study revealed no evidence of intrinsic pathology.

With a provisional diagnosis of cholelithiasis and obstruction of the common duct the patient was prepared for operation. The preoperative management consisted chiefly



FIG 2—Cholangiogram of Case 1

NOTE. The roentgenogram has been retouched for sake of clarity. The extra coil of the external limb of the "T"-tube has been obliterated.

of a high carbohydrate-high protein-low fat diet plus ten mg daily of intramuscular vitamin K. Following this regimen the patient's prothrombin time was 24 seconds, the control being 25 seconds.

On September 22nd, using spinal anesthesia, the patient was operated upon. The liver was atrophic, nodular, yellow-brown in color, with streaks of scar tissue between the nodules. No gallbladder could be seen. The stomach was normal, as was the head of the pancreas. The duodenum was adherent to the liver and common duct. The common duct was markedly enlarged, being approximately three centimeters in diameter (Fig 1). "White bile" was obtained from the common duct by aspiration. A large

stone, approximately two centimeters in diameter, could be palpated in the region of the ampulla of Vater. The extrahepatic ducts were thoroughly searched, but no structure resembling a gallbladder or cystic duct was discernible.

The stone was removed, and a "T"-tube inserted into the common duct after carefully probing the right and left hepatic duct.

A cholangiogram, October 3, 1945, showed the common duct to be patent, as the radiopaque material flowed into the duodenum. No structures resembling cystic duct or gallbladder were seen (Fig. 2). The patient was discharged from the hospital on the 17th postoperative day, having made an uneventful recovery. Following removal of the "T"-tube, cholecystography was attempted by the oral method, on November 23rd, to further rule out the possibility of an intrahepatic gallbladder, but no such structure was visualized.

**Case 2**—Through the courtesy of Dr. J. A. Shacter, we are reporting a second case of congenital absence of the gallbladder. On March 20, 1946, Mrs. M. P. entered Wesley Memorial Hospital complaining of pain in the right upper quadrant, and an intolerance to greasy foods. These symptoms had been constantly present during the past three years, but the patient also stated that even as a small child she was unable to eat the high-fat diet of her family table. The pain began as epigastric distress gradually increasing in severity. The onset was in the late evening with the pain lasting 12 to 48 hours. Bicarbonate of soda gave only partial relief. Nausea, belching, and flatulence accompanied these episodes. A weight loss of ten pounds in the past six months was noted. The past history revealed an appendectomy had been performed in 1928. The patient had been pregnant 13 times, and had been delivered of six living children. On physical examination, this 62-year-old white woman appeared to be in no apparent distress. Blood pressure 140/90, normal pulse. A few small, nontender lymph nodes were palpated in the left submaxillary area. The heart was of normal size, shape, and rhythm. The abdomen was obese, with a right lower quadrant scar. There was no tenderness or rigidity, and no masses or viscera were palpable.

The urine was normal. The erythrocyte count was 4,710,000 cells per cm<sup>3</sup>, and the hemoglobin was 14 Gm per 100 cc. The leukocyte count was 6,050 cells per cm<sup>3</sup>, and the blood Wassermann was negative. An oral hippuric acid test was within normal limits. The nonprotein nitrogen was 44.7 mg per 100 cc of blood. The total proteins were 7.05 Gm per 100 cc, with the albumin and globulin fractions 3.70 Gm and 3.35 Gm, respectively. Cholecystograms, made elsewhere, failed to visualize the gallbladder. The prothrombin time was within normal limits.

A preoperative diagnosis of chronic cholecystitis was made, and the patient operated upon on March 25, 1946. Careful inspection of the entire inferior surface of the liver failed to reveal a gallbladder. A small accessory liver lobe, 5 x 4 cm, was found at about the normal site of the gallbladder. The entire inferior and superior surface of the liver was readily palpated. Inspection of the liver surface itself failed to reveal what might have been a gallbladder buried within the liver substance. No cystic duct was found. Since the common duct was not opened, a "T"-tube was not utilized in an attempt to visualize an intrahepatic gallbladder.

**Case 3**—Mrs. M. W., a patient of Dr. Paul Rhoads and Dr. Arthur Metz, entered Wesley Memorial Hospital May 16, 1946. She complained of yellow color of the skin, intense itching, nausea, and malaise, all of four weeks duration. Although she had been troubled with "biliousness" for many years, the first right upper abdominal colic occurred in May, 1938. This episode subsided, and the patient was symptom-free until April, 1946, at which time a painless jaundice was noticed. The inventory of systems revealed selective dyspepsia to fatty foods, clay-colored stools, and dark-colored urine.

On physical examination, this 60-year-old, white female, appeared deeply jaundiced and superficial excoriations of the skin were noted. Except for an old right lower quadrant scar (removal of suppurative appendix and drainage of abscess in 1938), the only positive physical findings were those mentioned above.

The laboratory reported a normal blood count and hemoglobin level. The urine was dark in color, with urobilinogen present on several occasions. The stools were clay-colored and positive for occult blood. The icteric index was 1.48 units, with a four plus prompt van den Bergh reaction. On admission, the prothrombin time was 50 seconds, with 25 seconds for the control. Following vitamin K therapy the prothrombin returned to 20 seconds, with a control of 20 seconds. The albumin-globulin ratio was reversed. An upper gastro-intestinal study revealed no intrinsic pathology, and the electrocardiogram was within normal limits.

A preoperative diagnosis of neoplasm involving the extrahepatic biliary system was made. At operation, May 23rd, a thorough search failed to reveal a gallbladder or cystic duct. The extrahepatic ducts were slightly enlarged and very firm, as if invaded by a new growth. The pancreas appeared normal except for evidence of passive congestion. The surgical impression was primary neoplasm invading the common and hepatic bile ducts. Absence of the gallbladder and cystic duct was a coincidental finding. Since the common bile duct was not incised, cholangiograms were not possible.

**COMMENT.** For evident reasons, a preoperative diagnosis of congenital absence of the gallbladder is extremely difficult, if not impossible. This fact is well illustrated in our survey by the ratio of cases found at autopsy to those discovered at surgery. There is no group of symptoms or signs which are of value in making such a diagnosis. Roentgenographic visualization of the biliary tract is the most accurate diagnostic method known at present. The accuracy of this test, when properly conducted, is about 90 to 95 per cent.<sup>13</sup> However, when this method fails to produce any shadow whatsoever, congenital absence of the gallbladder is so rare that such a condition is not suspected, there being no reported case of the diagnosis made before operation or postmortem examination.

Should surgical procedure fail to reveal the gallbladder in or about its normal location, the presence of an intrahepatic location of this viscus should be ruled out. This can best be done, we believe, by retrograde cholangiography. Such procedure was reported in only three cases in the literature. Mackmull<sup>11</sup> injected a cadaver specimen, while Drenckhahn and Rogers,<sup>12</sup> and Dixon and Lichtman<sup>7</sup> illustrated the use of this method in the patient. This procedure of retrograde visualization of the biliary tree was carried out in one of the cases satisfactorily, and no evidence of the gallbladder or cystic duct was seen. Kehr mentions needling the liver and aspirating bile as proof of an intrahepatic viscus. We agree with Talmadge<sup>5</sup> who contends that aspiration of bile from the liver does not prove the presence of an intrahepatic gallbladder, inasmuch as bile may be aspirated from a dilated intrahepatic bile duct.

#### SUMMARY

1. The literature pertaining to congenitally absent gallbladder is reviewed.
2. A total of 71 cases of congenital absence of the gallbladder were reviewed and analyzed, 34 at operation and 38 at autopsy—one case appearing in both series.
3. We present three additional surgical case reports of congenital absence of the gallbladder. The absence of an intrahepatic gallbladder was proven by cholangiography in one case.

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# THE EFFECT OF ROTATION ON THE CIRCULATION OF THE LOWER EXTREMITIES

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EXPERIMENTS IN AVIATION MEDICINE with the "human centrifuge" produced marked changes in cardiovascular function. This suggested that centrifugal force might be used to drive blood through partially occluded arteries, and so increase the circulation to the lower extremities in cases of peripheral vascular disease. This was discussed with Mr Caleb Smith, an engineer and inventor of Seneca Falls, N Y, and he agreed to build the necessary apparatus for us to test this hypothesis.

## METHOD

The apparatus consisted of a chair (Fig 1), revolved by a 1 H P electric motor, and a Worthington "all-speed" drive, so that the speed could be varied from 0 to 60 RPM. Construction was such that the pivot could be released to balance the subject under static conditions by means of counterweights. This gave dynamic balance during rotation. It is apparent that in such a centrifugal force experiment the column of venous blood will be acted upon by the same force as the arterial supply, with resultant venous stasis and increased capillary pressure. If this persists, it may result in the accumulation of extracellular fluid. To counteract venous pooling, the chair was made to tip at rest, so that the feet might be elevated (Fig 2), thus, alternating a period of rotation with one of elevation.

Dizziness was an obvious disadvantage of such a procedure, so, to minimize it, the head was placed at the pivot point, and the mechanism was designed to control the rate of acceleration and deceleration.

It was difficult to decide how to test for circulatory change under the conditions of such an experiment. Plethysmographic measurements would record only volume changes, which might be misleading due to venous stasis. Capillary microscopy appeared impractical. Temperature readings during rotation presumably would be altered by air currents and the cooling effect of evaporation of sweat. It was felt, however, that if significant changes were produced, they could be recorded by skin temperature readings taken before and after rotation. A "dermatherm" wire thermocouple was used for these.

Preliminary experiments to determine the optimum conditions, such as speed of rotation, time of rotation, time of elevation of extremities, degree of nausea and vertigo, and effect of air cooling on the exposed foot were carried out. It was found that covering the foot with an oilskin bag during rotation produced no significant change, hence, this was omitted in later runs.

Two sets of experiments were undertaken. In the first, the subject was rotated at 36 and at 48 RPM for one minute, the chair was tilted up after each

rotation, and skin temperatures recorded at minute intervals thereafter. In the second series, the subject was alternately rotated at 48 RPM for two minutes and his legs elevated for one minute for a total of five times.

Skin temperature readings were taken from the plantar surface of the great toe in the first series and, in addition, from the plantar surface of the foot in the second series. The room temperature was kept constant at 68°–70°F. The 17 tested subjects were normal young males.

### RESULTS

In five cases the subjects were unable to tolerate the procedure, and the number of alternate rotations had to be reduced accordingly. In the first series



FIG 1—The revolving chair used in experiments to test the effect of centrifugal force on the peripheral circulation. The centering of the head over the pivot, the counterweights, and the driving mechanism are shown.

a slight increase in skin temperature was noted in four runs, and a slight decrease in two. With alternate rotation and elevation the temperature of the great toe increased slightly (1.6°C or less) in five tests and decreased slightly (2.3°C or less) in four, while the foot temperature increased (3.3°C or less) in seven and decreased (1.5°C or less) in two.

Nausea and vertigo were, as expected, found to be functions of the rates of acceleration and deceleration. In all cases these symptoms were present to a greater or lesser degree, and in five subjects it was necessary to curtail the experiment for these reasons. Foot cramps and tingling were common complaints, which were thought to be due to venous stasis or the presence of extracellular fluid. There were two cases of frank edema. In the first the subject

was unusually tall (6 ft 4 5 ins ) and, hence, was subjected to increased centrifugal force, while in the second case, the subject was spun for ten minutes continuously

The pulse rate, taken during and after rotation, did not reveal constant or unusual variation

COMMENT It is apparent from these results that significant temperature changes were not produced by the methods employed This is interpreted to mean that no appreciable increase occurred in the circulation The vasomotor effect of labyrinthine reflexes, or apprehension, may have played a part but were



FIG 2—The chair tilted back so that the feet may be elevated The usual sequence was a period of rotation at 48 RPM for two minutes, alternating with one minute of elevating the feet at rest, to avoid venous pooling

not apparent The occurrence of edema was obviously undesirable In view of this, and other disagreeable side effects, and with negative results, it was deemed unwise to subject patients to the procedure It is recorded only in order that others may be spared the expense and trouble of testing the hypothesis.

#### SUMMARY

Subjects were rotated in a specially designed revolving chair for varied periods and at varied RPM for the purpose of determining the effect of centrifugal force on the circulation of the lower extremity as measured by change in skin temperature

The results obtained reveal that no significant improvement of the circulation of the lower extremity is produced by this method This, combined with the undesirable side-effects of vertigo, nausea, and occasional edema of the extremities, makes it unsatisfactory for clinical trial

# SPONTANEOUS ILEOCOLIC FISTULA A COMPLICATION OF CARCINOMA

## CASE REPORT

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ENTEROCOLIC FISTULA is an uncommon, but not rare complication of carcinoma of the gastro-intestinal tract. A review of the literature reveals that most cases<sup>1, 2, 3</sup> were studied either late in the progress of the disease or at autopsy. The present case is reported to show that this complication may occur while the patient is still operable, a point brought out in recent reports by Catell and Mosely.<sup>4</sup>

Fistula formation, acute or chronic, may be produced by various etiologic factors. The more common is the benign ulceration as seen in the gastrojejuno-colic fistula. A second etiologic factor is trauma, due either to operation or to accidental injury. Carcinoma of the large bowel, a third factor, characteristically invades all layers, including the serosa. The neoplasm may then extend directly into any adjacent organ, ulcerate and, thus, form a fistula. On the other hand, the ulceration may first occur in the carcinomatous lesion causing a slow perforation. An adjacent organ, such as the ileum, may then form a block for the perforation. The ulceration continues and the neoplastic tissue invades the small bowel, thus, forming a malignant ileocolic fistula.

One of the outstanding findings in the study of these cases has been the occurrence of a distinct anemia. Barker and Hummel,<sup>5</sup> in a detailed study of macrocytic anemia in association with intestinal strictures and anastomosis concluded that the disease is a distinct entity and not a simple coincidence of "idiopathic" pernicious anemia and an intestinal lesion. They suggest the pathogenesis to be intimately bound up with stasis and putrefaction of the intestinal contents resulting in absorption of toxic substances. Surgical removal results in a cure, but intensive liver therapy may bring about clinical and hematologic improvement in some cases.

Roentgenologic examinations appear to be the most effective and reliable means of detecting the lesion. In many cases a routine study of the upper gastro-intestinal tract will not reveal any defect. In most instances the barium enema is most conclusive, and it is suggested that the insufflation of air into the colon or the double contrast enema be used.

The following case of spontaneous ileocolic fistula caused by carcinoma of descending colon is presented.

**Case Report**—J. C., a 47-year-old white male, entered the Veterans' Hospital, Rocky Hill, Conn., June 18, 1946, complaining of "pain beneath his shoulder blades and attacks of rectal bleeding and diarrhea" of approximately nine months' duration. He had



FIG 2.—Specimen removed at operation—combined resection of ileum and colon for ileocolic fistula complicating carcinoma of the colon. The probe is inserted into the fistula through the ileal opening. Note the size of the opening and the border of neoplastic tissue.



FIG 1.—Roentgenogram illustrating the direct anastomosis between the descending colon and ileum. Diverticula of the descending colon are noted at the site of the anastomosis.

lost 45 pounds, felt dizzy and weak, and had slight dyspnea. Seven months before admission, a gastro-intestinal series and an air enema had been done by his local physician. Diverticula of the colon were found and it was thought, at that time, that the diverticula caused his bleeding and diarrhea. His past history was essentially negative except for an appendicectomy performed in 1942.

Physical examination on admission revealed a thin, poorly nourished white male. There was a marked pallor to his skin, but his cheeks were flushed. On palpation, there



FIG 3—Same specimen as Figure 2, showing the probe inserted into the fistula through opening in the descending colon.

was a suggestion of a mass in the left side of the abdomen but this was difficult to evaluate because of the tenderness and pain of which the patient complained. The examination was otherwise normal.

*Laboratory Data*—Urinalysis—negative. Mazzini—negative. Sputum—negative. Daily blood counts revealed a macrocytic hypochromic anemia, with an average of 2.9 million red blood cells, and 45 per cent hemoglobin.

*Röntgenologic Findings*—Examination revealed a neoplasm in the region of the middle third of the descending colon. There was a direct communication between large and small bowel at the site of the obstruction (Fig 1).

*Preoperative Treatment*—1. Whole blood transfusions (five). 2. Concentrated vitamins intramuscularly. 3. High protein (Amigen), High carbohydrate diet. 4. Iron and liver therapy. 5. Sulfasuxidime. 6. Purgatives and cleansing enemata. 7. Miller-Abbott tube passed before operation.

*Operative Findings and Technique*—(Figs 2 and 3) At operation (7-30-'46) a large mass was found at the midportion of the descending colon. A loop of ileum was intimately attached to the large bowel. These lay parallel and were bound together in a side-to-side pathologic anastomosis, measuring 2 cm in diameter. Exploration revealed no other gross findings of note. The lesion was removed *in toto* to preserve the anastomosis. Bowel continuity was reestablished by a side-to-side anastomosis of the ileum and an end-to-end anastomosis of the descending colon. A complementary cecostomy was performed. Postoperatively, the patient was given sulfadiazine and penicillin.

The microscopic report (Fig 4) was that of adenocarcinoma of the large bowel, Grade II, with extension into the ileum, and the formation of a pathologic anastomosis. The lymphatics sectioned showed no tumor cells.

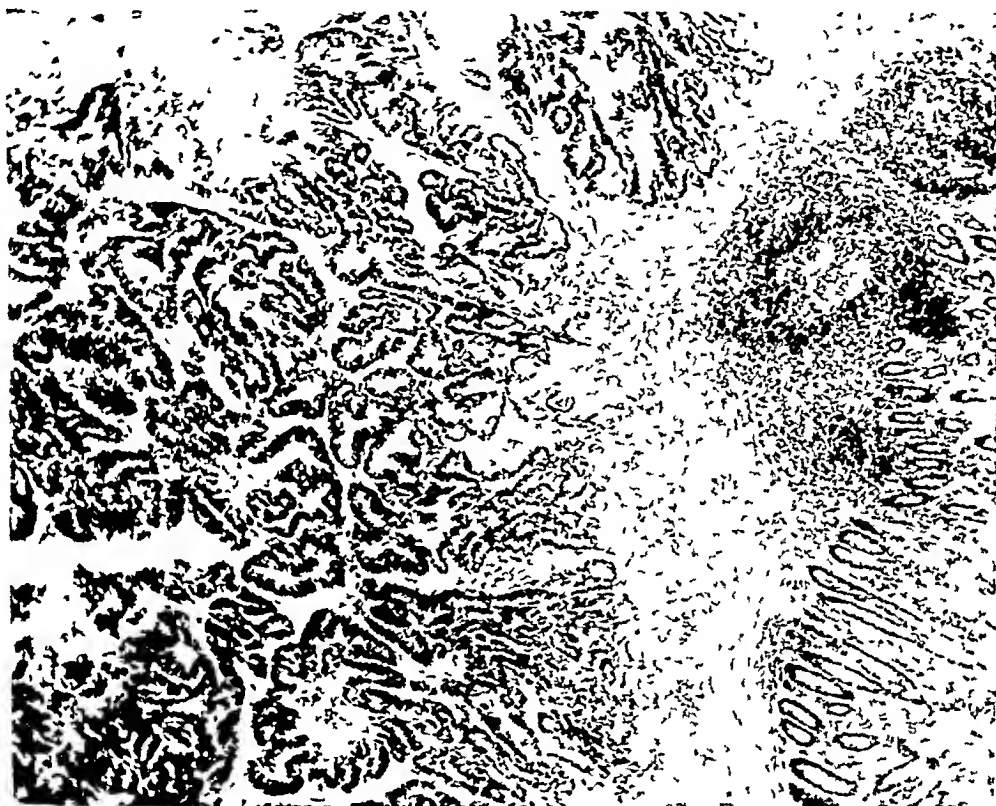


FIG 4—Microphotograph of block of tissue taken from the border of the fistula, showing normal ileal mucosa at the right, with invasion of neoplastic glands from a primary adenocarcinoma of the colon. (Hematoxylin and eosin stain  $\times 125$ )

*Progress*—The postoperative course was uneventful except for a small amount of drainage from a fecal fistula, which cleared up in a short time. Three and one-half months following operation he had gained 18 lbs, his hemoglobin was 82 per cent, and red blood count 4.42 million. On the most recent follow-up note, 11-12-'46, he states that he has no complaints and is doing part time work.

The patient reported to us June 10th. His weight is 190 lbs. The blood count is 5,000,000 red blood cells and hemoglobin 90 per cent. A repeat G I series was performed and showed no abnormal findings. He has no complaints and is back to full time work.

**COMMENT** There are several interesting findings in this case. Whereas, a review of the literature would lead one to expect a macrocytic hyperchromic type of anemia, this patient presented a macrocytic hypochromic type. The



explanation of this probably lies in the fact that the patient lost a considerable amount of blood during his episodes of bloody diarrhea. Despite the administration of five whole blood transfusions before operation, there was little appreciable improvement in the blood picture. However, after operation the blood picture rapidly returned to normal.

Bloody diarrhea is more commonly associated with malignancy than with diverticula, and should be thoroughly investigated before a definite diagnosis is established.

The previous operation (appendicectomy) is not a contributing etiologic factor because there were no adhesions found near the ileocecal junction. The part involved in the fistula formation was the midportion of the ileum.

#### SUMMARY

A case of combined resection of a portion of ileum and colon for an ileocolic fistula due to malignant disease has been presented. This case demonstrates the fact that this complication may occur before the malignant disease has produced widespread metastasis and, therefore, combined resection is feasible and may produce a cure.

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# ACUTE INTESTINAL OBSTRUCTION DUE TO ORANGE PULP BEZOAR

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THIS CASE REPORT is being made because a careful search of the literature fails to reveal any other case of acute intestinal obstruction due to such a cause. This was a case of acute intestinal obstruction due to the rapid ingestion of five fresh Florida oranges. While ordinarily this might have caused no difficulty, the present case had a dumping-stomach following gastric resection and a Pólya-anastomosis. Apparently, orange pulp was retained in the stomach and formed a bezoar. When finally expelled into the jejunum it was small enough to pass, but on arriving at the ileum, which is smaller in diameter, it produced obstruction.

Phytobezoars, composed of vegetable fibers, comprise about 40 per cent of the reported cases of bezoars. They are made up of stems, skins, fibers, or seeds, in the meshes of which may be included other food and epithelial detritus. Pyloric obstruction seems to be a predisposing factor. Rapidity of ingestion is important, bezoars probably being formed at one time, since no layers of accretion are found.

Persimmon seeds lead the list of etiologic agents, making-up the offending fibers in 75 per cent of the cases. Other substances reported are skins and seeds of prunes, plums, dried peaches or raisins, celery, cocoanut fiber and tobacco.

To have intestinal obstruction due to a phytobezoar is rare. Recently, however, three case reports have come from England of intestinal obstruction due to phytobezoars composed of dried peach.

**Case Report**—No 66915. Mr E. S. was admitted to the Hospital on 2-20-'46 at 7:20 P. M. The patient had awakened on the day of admission with colicky pains throughout the abdomen. The pains gradually increased as the day wore on, and had begun to localize in the right lower quadrant of the abdomen for approximately two hours prior to admission. A white blood count done at this time showed 9,200, with 75 per cent polys. By noon the patient had vomited only once. He had had two bowel movements during the day, one at 8:00 A. M., and one at 11:00 A. M. Nothing abnormal was noted about the movements, excepting that the cramps were aggravated following the bowel movement and there was an almost constant desire to go to stool. By 7 o'clock that evening, the patient was in considerable pain. The pain had localized quite well in the right lower quadrant of the abdomen. Temperature 99°F, pulse 90. There was two-plus rigidity of the lower abdomen, chiefly on the right side. There was tenderness over McBurney's point as well as rebound tenderness. Rectal examination was essentially negative. The patient had the scar of a previous gastric resection and a Pólya-anastomosis, which was done for a recurrent peptic ulcer in 1940. The remainder of the examination was

essentially negative *Postoperative Diagnosis* First, acute appendicitis, secondary possibility, perforating peptic ulcer

*Operation*—Dr Robert Bruce Malcolm Incision was made over the lower right rectus. The muscle was displaced laterally and upon opening the peritoneal cavity, there was encountered a considerable amount of slightly blood-tinged fluid. This fluid did not suggest the appearance of a perforation. The appendix was then located, exposed, and found to be normal, aside from its extreme length. Exploration of the upper abdomen showed that the gastro-enterostomy was apparently functioning well. There was no evidence of a perforation. On exploring the pelvis, a loop of ileum was brought up which was found to be markedly enlarged, greyish in appearance and about twice the normal caliber. This looked like a fibroma, but an incision made longitudinally on the antimesenteric border disclosed a mass which, when extruded, was found to consist of orange pulp. After further exploration the bowel was sewed with two layers of sutures and replaced. The appendix was removed. The abdominal wall was closed in layers without drainage. The patient had an essentially uneventful postoperative course.

## SUMMARY

A case of intestinal obstruction due to orange pulp is reported, which case is believed to be first of its kind in the literature.

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## MANAGEMENT OF COLOSTOMIES PERFORMED FOR WAR INJURIES

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THE PURPOSE of this communication is to report the experience with 67 colostomy cases in an Army hospital in England, and to draw a parallel between this experience and the trend of colon surgery in civilian practice.

Closure of colostomies in war casualties presented many difficulties not encountered in civilian practice. First among these were the patients with multiple injuries. Such injuries frequently produced superimposed infections, concurrent sepsis, impairment of vital organs, and general debility, all of which made the definitive surgery more hazardous. Secondly, the initial surgery was performed by surgeons in the forward area under difficult conditions so that the exact construction of the colostomy was often not clear to those who had to do the subsequent reparative work.

### PRIMARY SURGERY

The primary operative procedure recommended in injuries to the colon was simple exteriorization through muscle-splitting incisions along the course of the colon except in wounds of the rectosigmoid and the rectum where proximal loop-colostomy was recommended if the wound in the bowel could be closed. If not, complete diversion of the fecal stream was to be practiced. In general, these procedures best served the necessity for immediate exclusion of the injured segment from the peritoneal cavity and for the control of contamination by the pathogenic bacteria present in the bowel. In addition, these patients received parenteral penicillin and sulfa drugs (the latter both intraperitoneally and parenterally) during the postoperative course.

Even under the somewhat primitive conditions at the front physiologic balance in these patients was carefully restored preoperatively by the admin-

istration of whole blood, plasma, and solutions of electrolytes. This phase represents one of the great advances of war surgery. Much of the credit for mortality reduction in combat-wounded must go to the forward surgeons who not only did skillful emergency surgery but also practiced energetic resuscitation.

## ANALYSIS OF MATERIAL

Material for this presentation was collected over approximately one year in a General Hospital in England. It is summarized in Tables I and II.

TABLE I  
SITE OF INJURY IN 67 COLOSTOMY CASES

Right colon	13
Transverse colon	9
Left colon	15
Rectosigmoid	37
Rectum	7
	—
Total	81

It is quite apparent that at least 14 patients had multiple wounds since there was a total of 81 injuries in only 67 colostomy cases.

TABLE II  
SITE OF COLOSTOMY IN 67 CASES

Cecum	11
Right colon	6
Transverse colon	9
Left colon	13
Sigmoid colon	30
	—
Total	69

An additional decompressive cecostomy was performed in two patients who had left-sided colostomies, hence the apparent discrepancy in total number.

The types of colostomy seen at this hospital are classified in Table III.

TABLE III  
TYPE OF COLOSTOMY

Cecostomy	11
Double barrel (Mikulicz)	42
Loop	16
	—
Total	69

Table III shows that there were 11 cecostomies and 58 colostomies. Of the 11 cecostomies, five were complete exteriorizations and seven were catheter cecostomies. The exteriorizations were largely unnecessary. In all but one case of extensive damage and loss of the cecal wall, a catheter cecostomy after closure of the perforations would have been preferable.

The double-barrel colostomy and the loop-colostomy were the types most frequently seen. Too often they failed of the intended purpose or created troublesome complications for the following reasons:

(1) Muscle-splitting incisions containing bowel were placed too near the costal margins or the iliac crests, with the production of osteomyelitis of these structures

(2) Colostomies were placed too near coexisting cystostomies

(3) The colon was brought out through the exploratory incision and was not adequately mobilized. This led to retraction of the stoma, infection of the abdominal wall, intraperitoneal sepsis, sinus formation, and wound dehiscence. The error was particularly prevalent in colostomies of the transverse colon. In retrospect, it would have been better in many cases to make a transverse exploratory incision at a lower level and to bring out the damaged segment through an intramuscular incision higher up. If a vertical incision is to be used, the colonic loops should be brought out well laterally, for instance with the proximal loop on one side and the distal loop on the other. The important thing is to keep the colostomy away from the exploratory incision. In civilian surgery this is not always necessary, or even desirable, because proper precautions can be taken, but in war surgery the instructions were to remove the clamps immediately so that no colostomy could become obstructed through neglect. With feces spilling over a fresh wound, infection is inevitable.

(4) Occasionally, missile wounds of entry or exit were used for the colostomy. Such wounds invariably became infected and developed spreading cellulitis, adding to the difficulties of eventual reconstruction.

(5) In a few cases the loops of the Mikulicz colostomy had not been sufficiently mobilized so that the spur was too short, the bowel retracted, and the loops became rotated and partially obstructed. Blind crushing of such spurs is a particularly hazardous procedure because it cannot be determined beforehand whether there is interposition of mesentery or adherence of loops of small intestine.

(6) Loop-colostomies were occasionally found with edema and necrosis underneath because of glass rods or heavy rubber tubing. Such devices are no substitute for adequate mobilization of the loop. In other cases the incision through which the bowel had been brought out was too small, with resultant constriction and partial dysfunction of the stoma.

(7) Some loop-colostomies were found to have excessively large openings, often in the transverse axis of the bowel rather than in the longitudinal axis. Small wounds of the bowel that are incapable of being exteriorized (such as in the rectosigmoid) will heal satisfactorily if primary suture approximates the edges accurately and without tension. Under such circumstances the proximal decompressive colostomy with a small anti-mesenteric opening can be closed later by simple extraperitoneal suture.

(8) In wounds of the rectum and extensive wounds of the rectosigmoid with associated injury to the bladder, the urethra, and the bony pelvis, complete diversion of the fecal stream must be accomplished. Often the double-barrel colostomy did not do this, so that a revision had to be done later, with transverse section of the bowel and separation of the stomata.

(9) Drainage of the retroperitoneal and the pelvic space was not always adequate or it had been improperly established through the missile tract. Sepsis in these spaces is especially intractable and debilitating.

## RECONSTRUCTIVE SURGERY

The type of colostomy closure will be seen in Table IV

TABLE IV  
TYPE OF COLOSTOMY CLOSURE

Spur crushing	27
Spur crushing with decompressive cecostomy	2
End to end anastomosis	17
Simple inversion closure of loop stoma	9
Spontaneous closure	5
End to side anastomosis with resection of cecum	1
Colostomy not closed	8
Because of rectal wounds	4
Because of recto-urinary fistulae	2
Because of rectal wounds with osteomyelitis of the ischium	1
Because of rectal wounds with osteomyelitis of the ilium	1
Total	69

In general, these patients were considered candidates for reconstructive surgery when they were in physiologic balance and when the wound infection was under control.

In the restoration of physiologic balance the important criteria are hypoproteinemia and secondary anemia. Both should be corrected before surgery is undertaken.

In the treatment of the wound infection, the establishment of proper drainage and the application of carbamide were considered great time-savers. Carbamide is a strong lytic agent for devitalized tissues without noticeable effect on the physiologic processes of wound healing. It also deodorizes the discharges by the removal of the feeding ground of putrefactive organisms. Before surgery was undertaken, the wound was rendered at least macroscopically clean and the patient afebrile.

Following is a brief summary of the preoperative, the operative, and the postoperative routine.

*Preoperative*—(1) Proper preparation of the patient with blood and plasma, high-vitamin low-residue diet, parenteral feeding, and supplementary vitamins.

(2) Roentgenologic, sigmoidoscopic, and digital examination of the stoma, the colon, and the rectum.

(3) Low-residue diet and 2 Gm of sulfaguanidine every four hours day and night for five days before operation. Sulfasuxidine and sulfathalidine were not available when this work was done.

(4) Irrigations of both loops of the stoma the night before operation and again just before operation.

*Operative*—(1) Spinal anesthesia was used in all cases. With the patient anesthetized, the area of the colostomy was cleaned with soap and water and

the usual skin preparation carried out Into each stoma a gauze tampon on a silk thread was inserted

(2) The incision encircled the stoma and included all scar tissue The bowel loops were dissected free from the surrounding structures, including the peritoneum The peritoneal cavity was walled-off by warm saline packs The edges of the colonic stoma were freed from the rim of skin and scar tissue and the everted cuff of bowel was completely mobilized Adhesions walling-off the peritoneal cavity were disturbed as little as possible With careful preservation of the mesenteric blood supply, an open or closed anastomosis was then carried out, depending on which was the easier Gauze tampons were removed before suturing started The initial suture was 00 chronic catgut, continuous, the final suture was fine cotton interrupted After removal of the celiotomy packs, the sutured bowel was then restored to the peritoneal cavity In cases with an adequate spur or simple loop-colostomy, extraperitoneal closure was performed in the routine manner

(3) Crystalline sulfanilamide, 10 Gm , was introduced into the wound and the adjacent peritoneal cavity

(4) Wound closure was by through-and-through interrupted stainless steel wire sutures

(5) The wound was drained by a small wick of rubber tissue down to the peritoneum or to the fascial aponeurosis

*Postoperative* —(1) Levin tube when necessary for gastric and intestinal decompression

(2) Penicillin and sulfadiazine for the first 72 hours The sulfadiazine was given by vein during the first 48 hours, when the patient was unable to take fluids by mouth

(3) Intravenous fluids, plasma and blood transfusion as indicated

(4) Nothing by mouth for 48 hours, followed by gradually increasing diet

(5) Removal of the superficial drain after 48 hours and of the wire sutures on the 12th day

(6) Roentgenologic studies after three weeks

RESULTS OF COLOSTOMY CLOSURES

Table V records the results of 69 colostomy closures There was no evidence of postoperative peritonitis in any of these cases, and there were no deaths The complications were as listed Otherwise all wounds healed *per primam*, and the patients were discharged as cured

TABLE V  
RESULTS OF COLOSTOMY CLOSURE

Satisfactory		68
Fecal fistula with spontaneous closure	5	
Roentgenographic evidence of narrowed bowel lumen	7	
Abdominal wall infection	5	
Unsatisfactory		1
Total		69



In five cases a fecal fistula developed which lasted for several days and closed spontaneously, without further trouble

In seven patients, postoperative roentgenologic studies revealed a narrowing of the bowel lumen at the site of the anastomosis. These patients were all asymptomatic and gave no evidence of clinical obstruction. Six of these had



FIG 1—Colostomy brought out through major celiotomy incision resulting in wound infection, scarring and weakness of the abdominal wall following closure

been closed by crushing, and one by end-to-end anastomosis. Because the roentgenologic examination was made only four weeks after the operation, it is quite possible that reexamination at a later date will show resolution of the narrowing.

Five patients developed superficial infection of the abdominal wall, mostly because of the omission of drainage. Simple drainage of the abdominal wall effected cures in all these patients in a short time.

One patient was evacuated to the Zone of Interior with a persistent fecal fistula. End-to-end anastomosis had been performed in this case, probably under tension and in the presence of an extraperitoneal abscess.

All of these patients were either rehabilitated at a convalescent hospital or returned to the Zone of Interior for final disposition

COMMENT —The important observation in this series of cases was that the patients who had their colostomies closed by end-to-end anastomosis suffered less morbidity and had a shorter convalescence than those who were treated by the spur-crushing technic. In our patients, at any rate, end-to-end



FIG 2—Edema of colostomy stomata due to the presence of a glass rod beneath the openings over a prolonged period

anastomosis of the colon proved to be a safe procedure without any evidence of the once-dreaded peritonitis

This observation has a direct bearing on peace-time surgery. Primary anastomosis of the colon is being practiced more and more. Coller and Vaughan,<sup>1</sup> for instance, report very gratifying results, and their conclusions are fully substantiated by our observations. The only difference is that Coller and his associates adopted the technic as a primary procedure, whereas in our patients it was a secondary procedure the advantages of which were gradually realized.

What has made colonic anastomosis relatively safe in recent years? Probably a variety of factors

Modern chemotherapy must certainly be considered in this connection. In our patients, both penicillin and sulfa drugs were used, and it is our impression that they were of distinct value. The beneficial effect of penicillin on peritonitis has recently been stressed again by Crile.<sup>2</sup> As to the sulfa drugs in the preparation of the colon for surgery, we had to use sulfaguanidine



FIG 3—Colostomy placed in shall-fragment wound of entry. Abdominal wall infection was associated with a persistent purulent discharged from an infected sinus tract. A stab wound incision was made to allow free and dependent drainage of the infected sinus tract.

because sulfasuxidine and sulfathalidine were not available to us. This was unfortunate, because Poth<sup>3</sup> has recently reported that these newer drugs are greatly superior to sulfaguanidine in their effect on the bacterial flora of the colon.

More important, perhaps, than chemotherapy is operative technic. There are two errors to be especially avoided: an anastomosis under tension, and an anastomosis with a compromised blood supply. In our opinion, these factors were more decisive than whether the open or the closed technic was used.

Theoretically, the closed technic might be said to predispose to the formation of a diaphragm at least if the inverting sutures are too far away from the clamp, but it is interesting to note in this series that of the seven patients in whom postoperative roentgenologic examination showed some narrowing at the site of anastomosis, six had had their colostomies closed by crushing and only one by direct suture. It seems, then, that if a careful technic is used there is little to be feared in this respect.

Lastly, the treatment of the general condition receives much more emphasis now than formerly and it is here that the greatest advances have been made. Practically all patients need blood, protein, and vitamin therapy before they are ready for surgery. Once this has been attended to, it is surprising to see how quickly they overcome their infections and how well their wounds heal.

But regardless of whether it is because of better bacteriostatic drugs, better operative technic or better understanding of the physiologic processes, the conclusion is the same. In operations on the colon bacterial contamination is no longer the catastrophe that made surgeons formerly resort to devious procedures. With proper precautions the colon can be made as safe for direct anastomosis as the other parts of the gastro-intestinal tract. It is one of the contributions of war surgery to have underscored that fact.

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# MULTIPLE POLYPOSIS OF THE COLON WITH MALIGNANT CHANGE INVOLVING COLON AND APPENDIX

## CASE REPORT

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ALTHOUGH examples of multiple polyposis of the colon are not rare and carcinomatous change often occurs in connection with them, involvement of the appendix is almost unheard of. The case to be reported here, presents all of these features

**Case Report**—The patient, a female, age 35, was admitted to the Surgical Service of the New York Hospital complaining of painful and bloody prolapse of the rectum. Approximately four years prior to admission she became aware of the protrusion of a "small, soft, smooth growth" whenever she strained at defecation. At first, this was readily reduced spontaneously, but after several months it became necessary to practise manual reduction, which was accompanied by great discomfort. After a year's time the mass protruded four to five inches and seemed softer and more spongy than it had previously, bleeding continuously while it was prolapsed. One year ago, while seven months pregnant, the patient began to suffer from tenesmus and had 10 to 12 bowel movements daily. Each descent of the mass was accompanied by the loss of half a cupful of blood and an equal amount of mucus. After the delivery of her child, she felt weak and tired, and was found to have lost about 25 pounds in weight. She delayed applying for admission to the hospital for some time because of domestic and financial difficulties.

Her familial and past history were without any bearing on her present condition. She had always been frail, had rheumatic fever at the age of 18, and at 21 had a thyroidectomy performed for hyperplastic goiter. She had had five pregnancies and four normal deliveries. After her third pregnancy she suffered from a moderate cystocele and rectocele and from moderate prolapse of the cervix. Four years ago the cervix was amputated and the vaginal weakness repaired. Her last pregnancy was complicated by phlebitis of the right lower extremity which left it the site of a persistent but moderate elephantiasis.

**Physical Examination**—The patient was a pale, thin, "worn-out" woman who appeared 15 years older than her stated age. Aside from the elephantiasis, just mentioned, and the presence of moderate clubbing of the fingers which had been present for about 18 months, nothing of note was discovered on physical examination beyond those findings about to be described in connection with the rectum.

The tone of the external sphincter was notably reduced and four to five fingers could readily be introduced into the rectum, which was filled with soft, friable polypi that bled freely. Upon straining, a segment of the rectal wall 18 to 20 cm. in length was protruded. The snout-like protrusion, which apparently comprised all the layers of the organ, was covered with innumerable small polypi of a bright red color (Fig. 1). Both the extrusion and replacement of this mass caused intense pain, and 150–200 cc. of blood were discharged into the gauze dressing. After the mass had been replaced, the patient usually was quite exhausted.

**Laboratory Data**—On admission, the hemoglobin was down to 8 Gm., the erythrocytes to 3,100,000, the leukocytes were 7,500, with 76 per cent of polymorphonuclears.

and the serum proteins were 5 Gm per cent. Otherwise no significant findings were noted. The barium enema was not entirely satisfactory, but polyposis of the rectum and sigmoid was demonstrated and partially substantiated by proctoscopy. Roentgenography demonstrated a single polypus in the splenic flexure and many large polypi were noted in the hepatic flexure and its vicinity.

*Course*—The patient was treated by supportive measures, but in spite of a diet rich in vitamins, proteins and calories together with many transfusions of whole blood and infusions of amino-acids, her serum proteins had dropped in three weeks to 4.8 Gm per cent, the hemoglobin had increased only to 10 Gm and the erythrocytes to 4,100,000.



FIG 1—With the patient in the knee-chest position, after straining, a segment of the rectal wall, 18–20 cm in length, protruded. The snout-like protrusion, which apparently comprised all the layers of the organ, was covered with innumerable small polypi of a bright red color.

On her 23rd hospital day, a loop-transverse colostomy was performed in the left hypochondrium and after the stoma was completed, the rectum was occluded by means of a pyramidal dressing. Moderate ascites was noted at this time. By the 30th hospital day her serum proteins had begun to increase and were 5.8 Gm per cent.

On the 48th hospital day a polypus was excised from the splenic flexure, and biopsies were taken from those in the hepatic flexure through a sigmoidoscope introduced into the stoma of the colostomy. The last were reported as "adenoma malignum." The serum proteins had risen to 6.3 Gm per cent, and the hemoglobin to 12.0 Gm, the erythrocytes were 4,200,000.

*First Major Operation*—In view of the patient's notable improvement in physical condition, a right hemicolectomy and ileotransverse colostomy were carried out on the

71st hospital day, an aseptic anastomosis being performed between the end of the ileum and the side of the transverse colon within 10 cm of the open colostomy. No ascites was present. On palpation, the sigmoid contained polypi in the first 4 cm above the peritoneal reflexion.

*Pathologic Examination—Gross*—The specimen removed at this operation consisted of 7 cm of terminal ileum which opened into the ascending colon through a normal ileocecal valve, and of 37 cm of ascending colon. Attached to the cecum was an enormous appendix of fusiform shape, which measured 14 cm in length and about 4 cm in general diameter. It had the proportions of a gallbladder rather than an appendix. Through the



FIG 2—This photograph represents the cecum, appendix and part of the ascending colon. (1) Stump of the ileum. (2) Greatly enlarged and tumorous appendix. (3) Mass of polypi in the cecum, with a lighter annular area at the center, which represents the cecal carcinoma. (4) The largest of the malignant adenomas. Note the occasional smaller polypi in the ascending colon (right).

walls of the colon and appendix one could feel boggy masses of neoplastic tissue, but there was no infiltration of the parietes and the appearance of the external surface of the viscera was not noticeably disarranged.

Upon opening the specimen it was found that the entire ascending colon and cecum were covered, on their internal surface, by innumerable polypi of all sizes and shapes. Many of them had long pedicles, sometimes 4 cm in length, others were sessile, or relatively so. The heads of these polypi were mostly red, papillary and berry-like, and many of them were obviously of the type known as "adenoma malignum." Nested in the fundus of the cecum and surrounding the ostium of the appendix there was a mass of much firmer, grayer, fungating neoplastic tissue that was obviously malignant in nature.

Following the lumen of the appendix through the ostium it was found that there

was an uninvolved zone of normal-looking appendiceal mucosa lining the constricted neck of the organ. Distal to this the appendix was dilated into a fusiform sac, with a circumference of 7 cm at its widest point. Growing from the mucosa was a papillary tumor made up of innumerable coarse papillae, like those of a covecomb, they arose from a linear pedicle 3 cm, or more, in length, about 8 mm in width and running longitudinally along the wall of the lumen in its middle third. The tumor projected fully 2 cm into the lumen from its linear origin on the mucosa. It was soft, light grayish-brown and entirely unique in its appearance.

It is to be noted that there was no gross evidence of any physical connection between the cecal and the appendiceal tumors. (See Figure 2, gross specimen.)

*Microscopic Examination*—Sections from the cecal growth showed it to be a very malignant and rapidly growing carcinoma that was definitely invasive. Sections from representative adenomas in the ascending colon showed the usual appearance of adenoma malignum. Those taken from the appendiceal growth (Fig. 3) revealed it to be similar



FIG. 3—A field from the appendiceal carcinoma showing no close similarity to that from the cecal tumor. It resembles "adenoma malignum" of the lower intestinal tract and is fairly well-differentiated. ( $\times 140$ )

in every respect to the malignant adenomas in the ascending colon. It was not a frank adenocarcinoma like the tumor in the cecum (Fig. 4) and obviously was quite independent of it. It presented one unusual microscopic characteristic—its stroma was extremely rich in lymphoid tissue, possibly, to be interpreted as a result of the normally far more abundant lymphoid tissue in the appendix.

*Second Major Operation*—On her 80th hospital day the patient was subjected to a perineal resection of the polypus-bearing portion of her rectosigmoid, according to the method of Heuer. This operation has not formally been described. Briefly, the procedure is as follows. An incision is made around the anus at the mucocutaneous junction. The sphincter and muscle is carefully isolated and divided in the midline posteriorly. An incision is then made in the midline raphe beginning at the posterior border of the anus and carried backward to the junction of the coccyx and the sacrum. The incision is carried into the depths, until the posterior wall of the rectum is brought into view. The coccyx is resected to permit a wider exposure. Displacing the cut-ends of the sphincter and muscle lateralwards, the lower rectum is freed from the vagina or prostate anteriorly and deliv-



ered posteriorly into the wound. Laterally, the levator ani muscles attached to the rectum are divided. By careful dissection posteriorly, laterally and anteriorly, the rectum is gradually delivered through the perineal wound and the reflection of the peritoneum brought into view. The peritoneum is incised concentric with its attachment to the bowel and the peritoneal cavity opened. With this step, and, particularly, if the patient has a long sigmoid loop, the sigmoid can be delivered through the perineum. A point on the sigmoid above the level of the lesion is selected which is to form the new anus and, at this point, the tissues making up the mesentery are divided and the bowel cleanly isolated. The peritoneum is reattached to the bowel at a higher level, closing the peritoneal cavity. The levator ani muscles, if they have not been too near the pelvic wall, are reattached to the

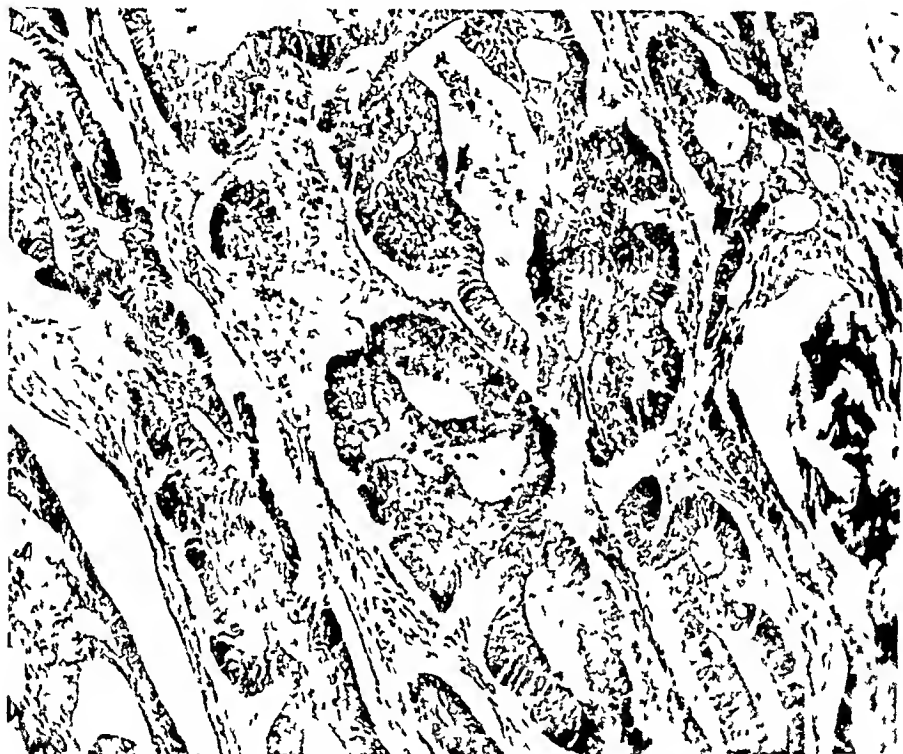


FIG 4—A field from the cecal carcinoma, which exhibits a multiacinar type of architecture, indicating considerable malignancy. For comparison with the illustration of the appendiceal carcinoma ( $\times 140$ )

intestine. The segment of delivered intestine is then swung forward within the sphincter ani muscle, the divided ends of which are then sutured with silk. The posterior wound is closed in layers with a rubber tissue drain placed in the pelvis along the curve of the sacrum. The intestine is cut across at the level of the skin and its cut-margins sutured to the skin as in the Whitehead operation. It is to be emphasized that the bowel, as reconstructed, should not be under the slightest tension so as to avoid the tendency to retraction upward into the pelvis.

A minimal infection of the dorsal aspect of the wound developed after operation, but promptly cleared under dakinization. The anal sphincteric control remained satisfactory.

*Specimen From Second Operation*—This consisted of a segment of rectum and sigmoid, measuring 18 cm. in length and 12.4 cm. in circumference (Fig 5). It is difficult to describe its appearance, as it was so thoroughly covered with polypi, of all sizes and shapes, that this would be unprofitable; the photograph is more informative. The polypi

grew in three main clumps, or crops, each of them some 9 cm in axial and 7 cm in circumferential diameter. They projected 5 cm into the lumen. One bunch of tumors had a pedicle 5 cm in length, 2 cm in diameter and a cauliflower-like top, measuring 7x5x6 cm.

Sections from representative polyps in this specimen showed them to be well-differentiated adenomas without any evidence of carcinomatous change. Thus, they were dissimilar from the growths in and about the cecum.



FIG 5—The rectum opened to show the polyposis of that organ. The two masses at the lower margins of the specimen represent the bisected portions of one large malignant adenoma. This was supported by a relatively tenuous pedicle.

*Subsequent Course*—The patient left the hospital on the 118th day after admission, the transverse colostomy stoma having been closed on the 109th day. She has been followed in the Out-patient Department for two months, has gained 15 pounds in weight, feels much stronger, and, more importantly, has one normal bowel movement daily. Her anal sphincter is strong and effective, and there is no prolapse of the rectal mucosa. She exercises her sphincter once daily by performing digital massage for five minutes, this has been her practice during the two months since her operation.

*Discussion*—When the patient entered the hospital it was evident that she was a poor surgical risk and was in no condition for an immediate operation. Attempts to replace lost tissue-fluids and serum proteins, employing

amigen, whole blood and plasma, were futile because of the large amount of blood and proteins lost with each movement of the bowels. A transverse colostomy, as a first procedure, placed the rectum at rest and improved the patient while it also permitted the removal of polypi from the splenic and hepatic flexures for microscopic study. Inasmuch as there was a reasonable suspicion of cancer in the ascending colon and since repeated biopsies of the rectal lesions were reported as nonmalignant, the former was attacked first. Careful preoperative preparation had cleared the ascites that existed at the time of admission.

The resected specimen revealed multiple polypi, both malignant and non-malignant, as well as a full-blown carcinoma of the cecum, in addition, a malignant adenoma of the appendix was found. This is unheard of in our experience.

Despite the proximity of the anastomosis of ileum and transverse colon to the left colostomy, movements of the bowels were controlled by means of a low residue diet and the administration of salts of bismuth.

A perineal-type of resection of the rectum and lower sigmoid, with preservation of the anal sphincter, was selected as the operation of choice in connection with her rectal lesions, as it was evident that the sigmoid was redundant and could be pulled down easily and the polypus-bearing area involved only the distal end of that segment of the colon. As biopsies from the polypi in this region invariably showed nonmalignant lesions, this type of operation was thought to be best calculated to overcome the patient's rectal symptoms and restore normal function. Whether the rectal prolapse was attributable to trauma to the sphincter during her several pregnancies or whether the polypoid mucosa acted as an intussusceptum and, thus, produced extrusion is not clear. Certainly, the fact that she had had a large rectocele and cystocele repaired and her cervix amputated, because of cervical prolapse, would suggest that weakness of the anal sphincter developed first, to be followed by chronic irritation and the production of multiple polypi. As there were polypi in equal abundance in the ascending colon and cecum, this explanation would seem faulty, and the hypothesis that prolapse was due to rectal polyposis appears to be more tenable.

Insofar as the carcinoma which occurred in this patient's appendix is concerned, the following points may be brought out, carcinoma of the appendix is a very rare condition, indeed, and a great deal of confusion has been caused by the inclusion of the so-called "carcinoids" in this category. Thus, when one endeavors to read up on the subject, many false clues are traced back, only to find that they lead to carcinoid tumors. Recently, Uihlein and McDonald,<sup>1</sup> of the Mayo Clinic, reported five cases of true adenocarcinoma of the appendix, the photomicrographic illustrations of which might have been taken from sections of the tumor reported in this paper. These authors divide appendiceal carcinoma into three categories, basing their observations upon an investigation of all the appendiceal carcinomas removed at the Mayo Clinic, between the years 1910 and 1941. There were 144 specimens of which 127 (88.2 per cent)

were carcinoids, 12 (83 per cent) were cystic carcinomas, and five (35 per cent) were colonic in type, resembling the adenocarcinomas of the colon. To the last category they added four new cases, bringing the number up to a total of nine, at the time of publication of their paper in 1943. These figures give an excellent idea of the rarity of the colonic type of appendiceal carcinoma. The authors have tabulated the usual sites of the various types, the colonic is found to arise in the base or tip of the organ and, occasionally, to invade the cecum. One of their recent cases, however, showed the tumor in the middle third of the organ.

Association with multiple polyposis, or carcinoma primary in the cecum, is not mentioned by these or other authors consulted, apparently, it is extremely rare. Ewing<sup>2</sup> dismisses the subject by remarking that appendiceal carcinomas are usually bulky adenocarcinomas that resemble those of the colon. Apparently, from reports which one may find on the subject, these tumors are usually well-differentiated, show a variable number of mitotic figures, and, may, on occasions, metastasize to lymph nodes and the liver. The Mayo group give them a Broder's grading of I, which would correspond with the histologic criteria in our case very excellently. Their group of "cystic carcinomas," in which there are malignant changes in the mucosa of an appendiceal mucocele, does not interest us here. One might question including it under true carcinomas, just as one might doubt the advisability of including argentaffin carcinoids in that category.

#### SUMMARY

An unusual case of multiple polyposis of the colon, cecum, vermiform appendix and rectum is presented. There was marked prolapse of the rectum and the patient had become very much debilitated by loss of blood. This was successfully overcome by (a) preoperative supportive treatment, (b) careful timing of the operative procedures, including transverse colostomy, ileotransverse colonic anastomosis, hemicolectomy, perineal resection of the rectum, and lower sigmoid, and (c) closure of the stoma of the transverse colostomy.

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# THE EFFECTS ON VENOUS ENDOTHELIUM OF ALTERATIONS IN BLOOD FLOW THROUGH THE VESSELS IN VEIN WALLS, AND THE POSSIBLE RELATION TO THROMBOSIS

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MOST CLINICIANS are increasingly conscious of the menace of venous thrombosis and possible pulmonary embolism. Why thrombosis occurs must surely be known before effective prevention of the possible results can be attained. It is to the end of determining causes of clotting in veins that these experiments have been undertaken. They are not wholly satisfactory, since in dogs there is no transition period between buoyant good health and progress to death as occurs in humans.

In this paper, the attempt has been made to introduce the circulation of the vein walls as a factor in the problem of thrombosis. This is a new approach and may be profitable.

When such lesions as so-called "spontaneous" thrombophlebitis or phlebotrombosis are discussed, it is assumed that three factors are relevant to their etiology, and that a given instance of "spontaneous" venous thrombosis or phlebitis is due to an imbalance of any two of them. These factors are (a) alterations in the quality or quantity of blood constituents, (b) alterations in the rate of flow of blood in the veins, and (c) alterations in the endothelial coats of the veins. This paper is devoted principally to a consideration of the last-named factor, the vein walls, and some of their physiologic relationships.

Experimentally, venous thrombosis has been produced by damaging vein walls in various ways, such as crushing, stretching, scratching off endothelium, or injecting sclerosing agents. These factors scarcely resemble any pathologic process which may occur in postoperative or postpartum patients, or in individuals afflicted with systemic infections, cardiovascular disease, or other debilitating disorders. A great amount has been written concerning the nutrition of the walls of arteries,<sup>1</sup> relatively little work has been done on the nutrition of vein walls. Discussions in the literature reveal three schools of thought: (a) that the inner layers of the vein wall are nourished by blood in the vasa venarum, (b) that the inner layers of the vein wall are nourished by blood in the parent lumen, and (c) combinations of these two.

No matter what the source or sources of vein-wall nutrition, it is probably necessary to distinguish between the supply of oxygen and the supply of other metabolic necessities, such as water, glucose, amino-acids, and inorganic salts. Such a distinction is advisable, for oxygen, unlike foodstuffs, must be constantly supplied since facilities for its storage in tissue or tissue fluid are

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practically nonexistent. Certainly, the organism as a whole reacts much more promptly to oxygen lack than it does to lack of nutriment, and if venous endothelium is at all comparable to capillary endothelium it should suffer from hypoxia in a somewhat similar fashion.

## THE ANATOMY OF VASA VENARUM

### 1—TECHNIC

Since few investigators have studied the vascular supply to vein walls, it was necessary to spend much time on this topic. In the present work, the first attempts to demonstrate these tiny vessels involved the usual injection technique, which were only partly successful. A new technique was then devised for holding vein segments after they had been removed, and the benzidine staining reaction was employed to outline the vasa venarum. All experiments were carried out on dog veins. Depending on the size of the animal and the available length of the vein to be studied, a segment, 3 to 12 cm., was carefully

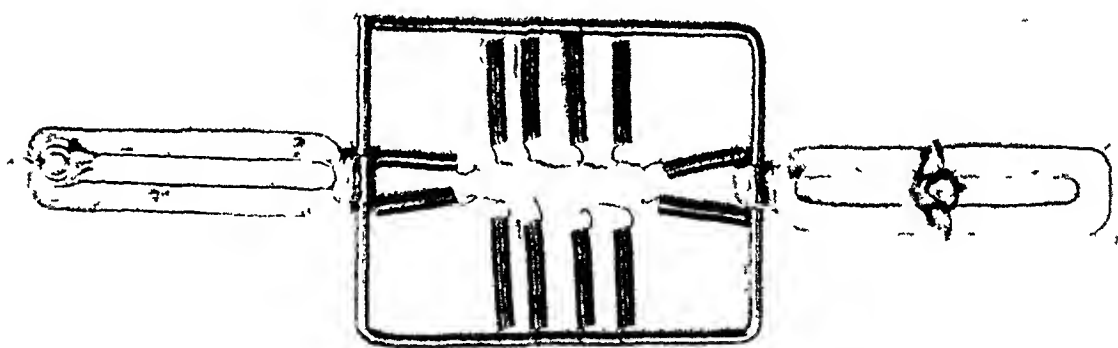


FIG 1—Apparatus used for holding vein segment flat while being stained, dehydrated, and cleared. The tissue is secured by the stainless steel springs in the frame made of stainless steel rod, which, in turn, is held by adjustable brass clips while the specimen is being attached.

dissected free, and a glass cannula inserted in its distal end and the lumen washed through with Ringer's solution at body temperature. Ligatures, which had been previously placed at either end of the isolated segment, were immediately tied, imprisoning Ringer's solution in the vein lumen. The segment was then removed, and kept moist with warm Ringer's solution while it was being opened longitudinally and stretched out flat in a rectangular frame by small springs (Fig 1).

The frames used were made of stainless steel rod, 3.17 mm in diameter, bent into rectangles 7 cm wide and from 7 to 15 cm long, the various lengths being necessary to accommodate various lengths of vein segments. The springs used were made of stainless steel wire 0.010 in thick. Each spring consisted of 50 turns of wire, and was 2.2 cm long and 4 mm outside diameter. A linear force of 15.3 Gm stretched a spring 1 cm. Simple loops lying in the same plane were bent on each end of a spring, and one or both loops were

sharpened to a fine point with a small motor-driven hand grinder so that they would easily pierce vein walls

To eliminate excessive pull on the vein segment being mounted, the spring should not have too much tensile strength, and the frame size should not be unduly large in relation to the size of the specimen. To hold the frames steady while the vein segments were being attached to them, two adjustable clips of half-hard brass were mounted on a flat tray so that the curved tips of the clips could be fitted over the ends of the frames and locked in place by wing-nuts

To mount a given vein, a rectangular frame of suitable size was placed on the flat tray, and the brass clips adjusted and locked in position to hold it in place. The portion of vein to be attached to the frame, having ligatures at each end and Ringer's solution in its lumen, was then placed on the tray within the frame, and kept well-moistened with warm Ringer's solution. The sharp end of a small spring was then thrust through the loose cuff of vein wall at each end, outside the ligatures. By means of small scissors and forceps, the vein segment was then opened longitudinally, care being taken that the point of the scissors within the lumen did not damage the opposite vein wall.

Once the vein is opened throughout its length, other springs were alternately hooked through the lateral edges of the wall on either side, and the outer, free end of each spring was attached to the side rod of the frame. These springs were placed 5 to 8 mm apart.

Then each of the four corners of the specimen was attached to the ends of the frame by springs, after which the tissue contained in the ligature was cut off, removed from the spring holding it, and discarded. These two springs at either end were then hooked through the midpoint of the end of the vein segment. Once the tissue is thus secured, the entire frame was turned over, so that the endothelial surface of the vein faced downward. By means of scissors, forceps, and magnifying spectacles or a dissecting microscope, any clumps of excess adventitial tissue were dissected away. This was done so that the vein segment would be flat on a glass slide when finally mounted in balsam. It must be done with meticulous care lest the vasa venarum be damaged.

The entire preparation was then immersed in warm Ringer's solution and washed by gentle agitation for one or two minutes, after which a similar washing was carried out using 5 per cent dextrose. It is inadvisable to wash these specimens by directing running streams of solutions on them, for the force of the stream may damage the tissue. This is of utmost importance when the endothelium is to be stained and studied.

Each preparation was then immersed in a solution of benzidine for 15 minutes. A mixture suggested by Sjöstrand<sup>2</sup> was used. This was prepared by combining two solutions, as follows. Solution A contained 0.9 Gm of benzidine base in 60 cc of 95 per cent ethyl alcohol. Solution B contained 3 cc of 30 per cent hydrogen peroxide in 120 cc of 70 per cent ethyl alcohol. Solutions A and B are then mixed, and the vein segments placed in this mixture.



FIG 2—Photomicrograph of blood vessels in wall of normal jugular vein of dog, stained with benzidine ( $\times 210$ )



FIG 3—A portion of Figure 2 ( $\times 550$ ) Note stained red cells in vessels and tortuous course of partly filled capillary



The benzidine, by selectively staining red blood cells, can outline the vessels in which they are contained. This technic, first used by Lepehne,<sup>3</sup> was later employed with various modifications by Sjöstrand,<sup>2</sup> by Pickworth,<sup>4</sup> by Campbell, Alexander, and Putnam,<sup>5</sup> and by others, to outline small blood vessels in sections of brain, spinal cord, and other viscera. It stains the blood cells an amber to dark brown color, depending on the duration of staining and the amount of blood present in a given vessel.

Each specimen was again washed in 5 per cent dextrose, and then fixed in 10 per cent neutral formalin for 12 to 18 hours, following which it was dehydrated by successive immersions in 70 per cent, 80 per cent, 95 per cent,



FIG 4—Cross-section of wall of normal jugular vein of dog, stained with benzidine and counterstained with hematoxylin and eosin. The endothelial surface is shown in the lower right corner (A), and the adventitial surface in the upper left corner (B). Cut-ends of three vasa vasorum are shown in the inner part of the adventitial coat.

and absolute alcohol, allowing it to remain one-half hour in each of the first three solutions, and one hour in the absolute alcohol. Clearing was carried out by immersion in oil of wintergreen for 12 to 18 hours.

As containers for the various solutions in which these preparations were immersed, rectangular glass dishes, ordinarily used for food storage in household refrigerators, served admirably. Their inside dimensions at the bottom are 19 cm. in length, 8 cm. in width, and 6 cm. in depth, and each is equipped with a glass cover.

After clearing, each specimen was removed from its frame, by securing the frame on the flat tray with the brass clips and cutting off the margins of the segment where the springs pierced it. The remaining portion of flat, stiff, transparent vein wall was then mounted in balsam between a glass slide and a long cover slip.

2—ANATOMY

Preparations so made admit of examination with a hand lens or a microscope, and a large area of vasa venarum can be studied by looking directly down upon it (Figs 2 and 3). The vessels vary in diameter from those of true capillary size with diameters of 10 to 20 $\mu$ , to those of arteriole or venule proportions having diameters of 60 to 75 $\mu$ . An occasional arteriovenous anastomosis is visible. The richness of these plexuses is impressive, an opinion also expressed by Köster,<sup>6</sup> in 1875, who, in commenting on the structure of blood vessel walls and inflammation of veins, remarked "The vasa nutritia (of veins) are extraordinarily more numerous than is ordinarily represented, and supply quite small veins, whose wall one thinks would surely be without vessels."

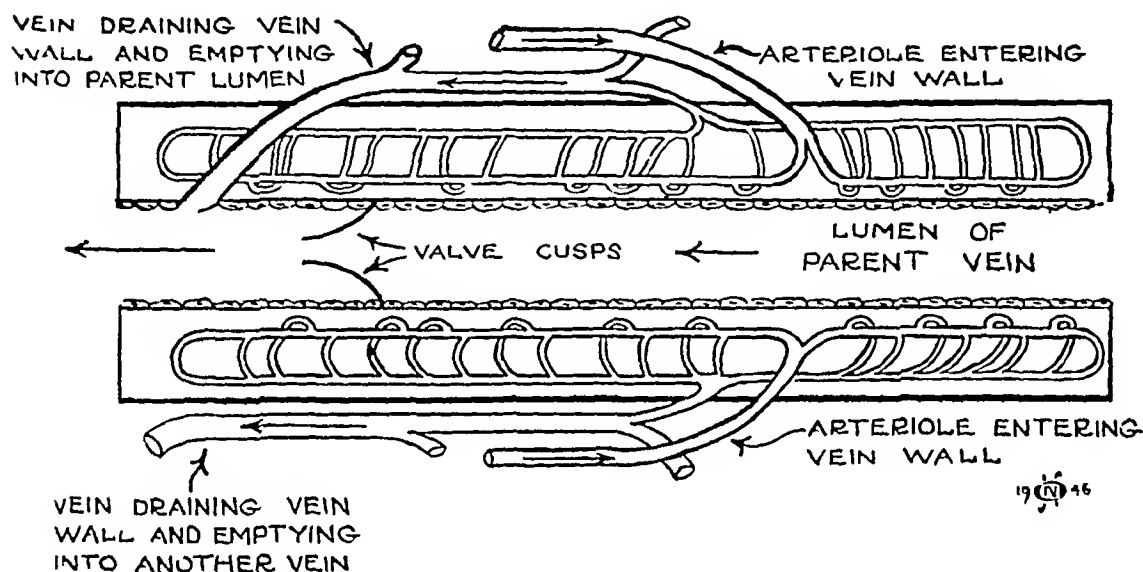


FIG 5—Diagram of blood vessel pattern in vein walls

In specimens so studied, vasa venarum have not yet been seen in the media or in the intimal layers of the vein wall (Fig 4). This justifies no conclusions, however, that tiny vessels do not penetrate into the media or intima, for demonstration of such vessels may be prevented by lack of penetration of the benzidine stain deeper than the inner part of the adventitia, or because certain vessels are empty at the time of staining. It may well be that staining for longer periods will permit greater dye penetration and, consequently, outline vessels in the deeper vein layers.

Study of the patterns of blood vessels in vein walls have led to certain concepts about their origin, distribution, and destination. As diagrammed in Figure 5, they arise as branches from arterioles present in perivenous connective tissue, these arterioles, in their turn, having come from neighboring arteries. The arteriolar vasa venarum enter the venous adventitial coat, and then divide and subdivide to form a rich capillary network whose depth of penetration is still uncertain. It is important that in all specimens so far

studied there is no evidence that the venous capillaries or the venules in the plexuses in vein walls empty directly into the parent lumen, but, rather, that the venous capillaries form venules which emerge from the adventitia of the vein wall usually as *venae comites* for the entering arterioles, and then empty into the veins which run in the loose perivenous connective tissue. These veins, in turn, then join others in the vicinity, and finally empty as a true tributary into some other vein, or, if it be in an extremity, it may empty into the parent vein at some more proximal site.

A consideration of the pressures acting within and around a vein attest to the efficiency of such a plan. If venous capillaries in the *vasa venarum* of a vein wall drained directly into the parent lumen, their emptying would be hindered by any local increase in intravenous pressure, and, unless they were all valved, actual regurgitation might occur into them if local intravenous pressure rose.

In a system so arranged that venous *vasa venarum* in vein walls emerge from the adventitia, and drain into surrounding veins, later emptying into the parent vein at some distant site, local increases in intravenous pressure can have no harmful, and may actually have a helpful effect on their emptying. For a rise in intravenous pressure in a given vein segment may, by exerting force on a vein wall from within outward, tend to massage blood out of the venous *vasa venarum*, and since they can drain into surrounding veins in a plexiform arrangement, their flow would not be seriously hampered. Again, if contraction of local muscle compressed a given vein segment such pressure would tend to empty the veins in the vein wall and perivenous tissue, and at the same time force the blood in the parent lumen centralward. Thus venous *vasa venarum* would have no obstruction put in their way, and their drainage might even be aided by an aspiration effect occurring at the site where the tributary they help to form opens into the parent vessel.

#### CHANGES IN ENDOTHELIUM FOLLOWING ALTERATIONS IN BLOOD FLOW IN VASA VENARUM

An anatomic discussion of *vasa venarum* should be complemented by further studies to learn something of their function, particularly the part they play in vein wall nutrition. Accordingly, experiments were devised to study the effect on vein walls, principally on the endothelium, when the blood supply *via* the *vasa venarum* was cut off. It is not a difficult matter to dissect a vein segment free from all its surrounding tissues, to permit the vein to lie thus isolated for varying periods of time, and then to study the endothelial changes which may have occurred. In such experiments the dissecting technic must be meticulous in order that the effects of trauma will be kept to a minimum. Second, when a vein is carefully isolated, the nerves and lymphatics as well as blood vessels of the vein wall are divided. Third, if such studies of endothelium relied upon orthodox cross-sections only, it would be difficult to visualize in proper perspective a sufficient expanse of endothelium to derive an adequate picture of any changes which might occur. For this reason a new

approach was employed, and the vein walls mounted flat so that the inner layers could be examined microscopically after staining with silver nitrate

When the time arrived for the termination of each experiment, a right-angled cannula, as wide-mouthed as the vein would admit, was inserted into the proximal end of the isolated vein segment, and the blood emerging from the vein was collected so that it could be immediately examined for clots, and minute volume determined and compared to normal flow. These vein segments were not washed out with Ringer's solution, lest endothelium be artificially damaged. They were ligated at either end, removed, opened longitudinally, and mounted flat in the small frames as previously described. Excess adventitia was trimmed away, and the segments were washed in Ringer's solution and 5 per cent dextrose, as discussed above. The Ringer's solution was used to remove any blood from the endothelial surface, and the 5 per cent dextrose which was preferred to distilled water because it is isotonic, was used to wash away any chlorides remaining from the Ringer's solution and, thus, prevent the formation of silver chloride when the silver nitrate was applied.

Since, in these segments, the endothelium and not the vessels in their walls was to be examined, they were stained with 1:250 silver nitrate solution. To do this, each frame was placed over a beaker or Petri dish, and a few drops of silver nitrate placed gently on the endothelial surface so that it would not run on to the lower or adventitial surface. The stain was permitted to remain 30 to 60 seconds, the vein segment being gently agitated during this time. It was not found necessary to formally expose the vein to a source of ultraviolet light after applying the silver nitrate. Sufficient staining of intercellular lines occurred even when the silver nitrate was applied at night under artificial light.

The staining was followed in each instance by fixation, dehydration, clearing, and mounting in balsam, as previously described.

With this technic a large flat area of endothelial surface can be examined microscopically by looking directly down on it, and it has often been possible to examine 5 sq. cm. of endothelial surface in one preparation—more than could be studied in several thousand cross-sections made by the usual microscopic technic.

So far as is known, this approach to the study of venous endothelium has not been previously employed. Langhans,<sup>7</sup> in 1866, did make mention of horizontal sections used in studying aortic endothelium, but details of how he made his preparations are lacking. He also stained these specimens by immersing them from 5 to 24 hours in 0.4 per cent solution of silver nitrate. This salt was first employed as a tissue stain by Flinzer,<sup>8</sup> who, in 1854, used it to outline the cells of the cornea, but, according to Mann,<sup>9</sup> silver staining was made a general histologic method by von Recklinghausen in 1860. Since that time it has been used in various ways by various investigators. The general principles, as well as the technical details of its use, have been summarized by Ranvier,<sup>10</sup> by Mann,<sup>9</sup> and by Lee.<sup>11</sup>

When applied to venous endothelium, silver nitrate stains the intercellular cement substance a dark brown to black color, which Rabi<sup>12</sup> has suggested is due to the formation of a silver proteinate. He feels that it was not metallic silver, for it was soluble in sodium hyposulphite. In normal endothelium, the cells themselves do not usually stain, but they are nicely outlined and form a delicate mosaic pattern (Figs 6 and 7).

Normal venous endothelium apparently varies somewhat in its appearance. The intercellular lines may vary in thickness, nuclei of the endothelial cells are sometimes visible, and whether this is due to their being stained, *i.e.*, a positive shadow, or due to their not being stained while cytoplasm is stained, *i.e.*, a negative shadow, is not clear. In some preparations where the vein wall has not been damaged, fine, roughly parallel lines running transversely to the long axis of the vein are visible through a superimposed endothelial pattern. At the present time, these are believed due to the silver nitrate solution penetrating through the endothelial layer and staining some cement-like substance or ground substance between the circular muscle fibers. Some of these variations may be associated with variations in the nutrition or age of the dogs used, differences in oxygen saturation of venous blood, and inequalities in technic in removing and staining the venous segments.

The first series of experiments to be discussed is concerned with changes in the inner layers of the wall in veins which are not obstructed but which are dissected free from all blood supply to their walls. After gently separating a vein from all its surrounding tissues, the line of cleavage being in the inner part of the adventitia, rubber dam is sutured loosely around the isolated portion to make certain that it remains separated from its bed. The wound can then be closed and the vein permitted to remain *in situ* for periods varying from three to 48 hours.

When such an experiment is continued for six hours, and the vein segment removed, stained, and mounted as described, the inner coats, when viewed microscopically at low power (Fig 8), show some areas where the endothelium looks little, if at all, different from normal. However, it is more granular, many nuclei are visible, and they have the appearance of negative shadows. At various places, round black spots occur on the intercellular lines, their greatest incidence being at junction points. In other areas, the endothelial pattern is absent, being replaced by roughly parallel black lines which run at right angles to the long axis of the vein. In some instances endothelial loss is focal, consisting of absence of only a few cells, the space being filled with the black parallel lines or with a homogeneous black area studded with small round vacuole-like structures. These clear tiny circular structures have not yet been identified. The black transverse lines, however, are felt to represent some substance lying between circular muscle fibers, possibly similar to intercellular cement or ground substance, and which has been stained black by the silver nitrate, because the overlying endothelium has desquamated, allowing the silver to come in direct contact with it.

Consideration has been given to the suggestion that where the black

FIG 6

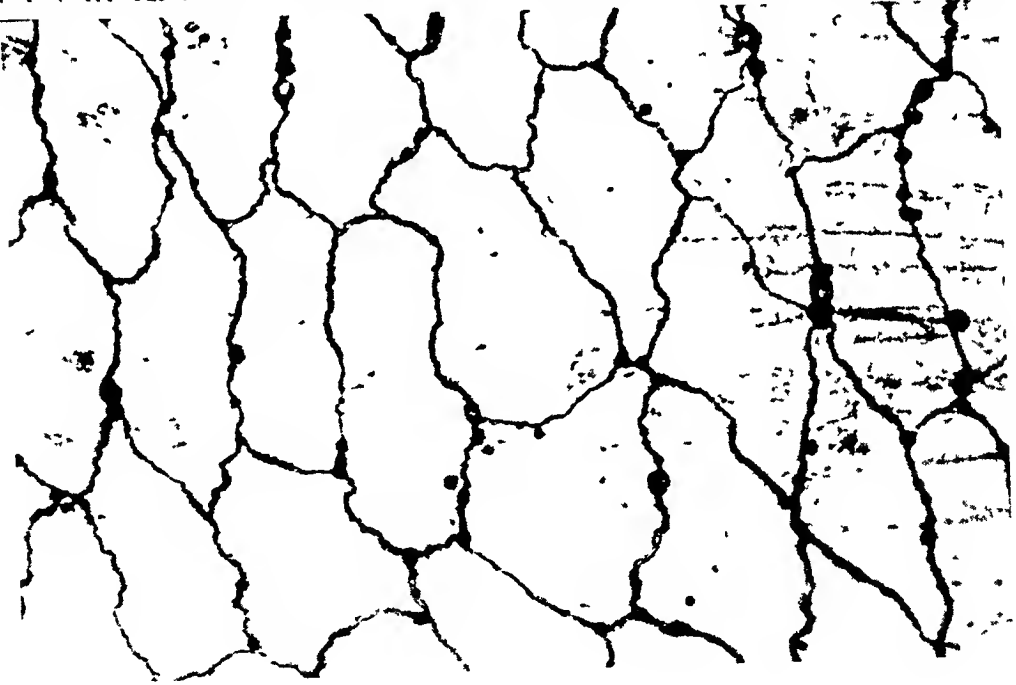
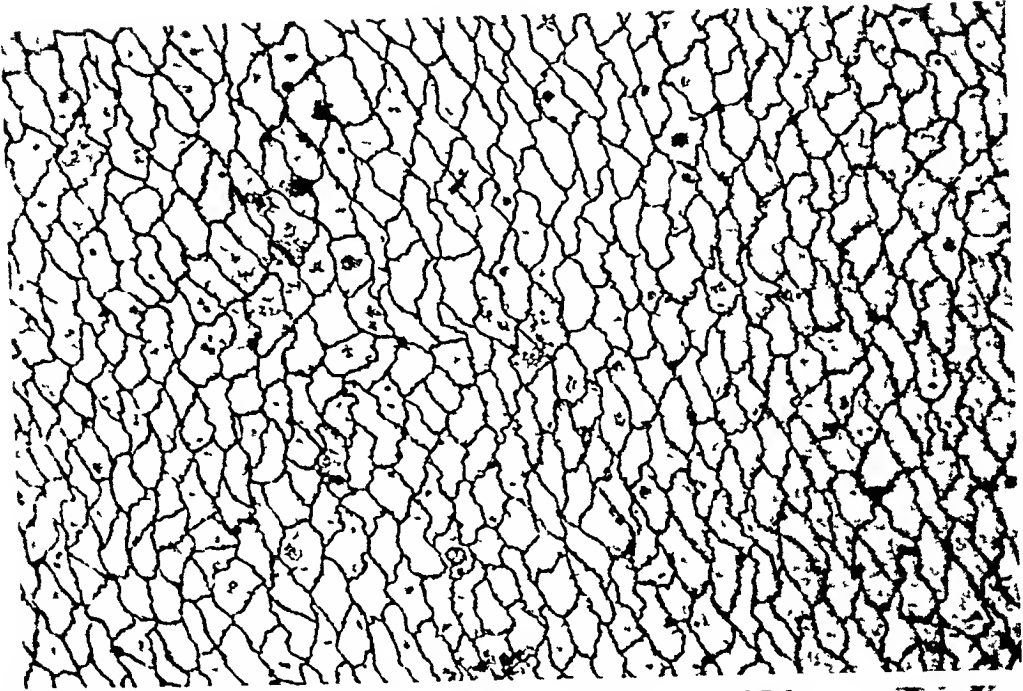


FIG 7

FIG 6—Photomicrograph of the endothelium of a normal jugular vein of a dog, stained with 0.4 per cent silver nitrate solution ( $\times 210$ ). Irregular black granular deposits are present in some areas. The round black shadows present on some cells are not nuclei but probably masses of protein material stained with silver nitrate. An occasional nucleus is visible as a round, relatively light zone.

FIG 7—A higher magnification ( $\times 550$ ) of a portion of Figure 6. Note the round, relatively light cell nucleus in the right upper part of the picture, as well as the variation in the width of intercellular lines. A few black parallel lines are seen beneath the endothelium, running at right angles to the long axis of the vein wall.

FIG 8

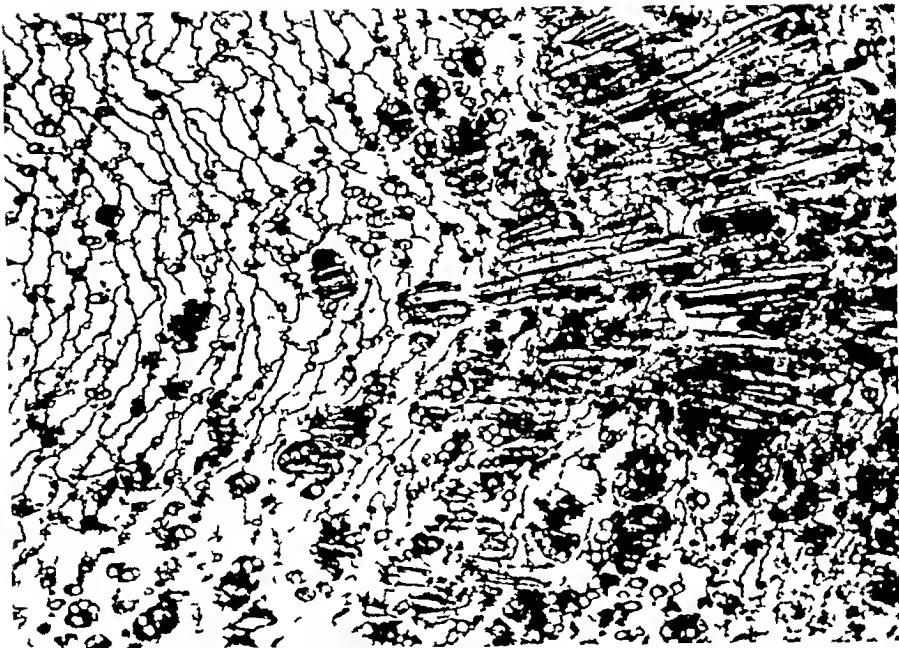


FIG 9

FIG 8—Photomicrograph of endothelium of dog's jugular vein after the vein segment had been isolated from all blood supply to its wall for six hours. Stained with 0.4 per cent silver nitrate solution ( $\times 210$ )

FIG 9—Photomicrograph of endothelium of dog's jugular vein after the vein segment had been isolated from all blood supply to its walls for 13.5 hours. Stained with 0.4 per cent silver nitrate solution ( $\times 210$ ). Black parallel lines, running at right angles to the long axis of the vein, are visible beneath the endothelial outline.

parallel lines are visible and endothelial cells are not, the phenomenon may be due simply to dissolution of cement substance, allowing the silver stain to penetrate through and react with the subendothelial tissues, leaving behind the unstained and, therefore, invisible endothelial cells, and that the observer may, thus, get the erroneous impression that the cells were absent. That these cells have desquamated is conclusively shown in conventional cross-sections of the vein walls.

In another experiment, continued for 135 hours, the endothelium was apparently still present, but the black transverse lines could be seen lying beneath it (Fig 9). It seems possible that, in this particular vein, the silver nitrate penetrated through and between the endothelial cells, and stained some substance between the circular muscle fibers. In some areas, the cell nuclei are visible while in other areas they are not, yet in all places the subendothelial tissues are uniformly stained. It is reasonable to conclude that in some sites the silver nitrate passed through the cell bodies on its way to deeper layers, staining nuclei or cytoplasm *en route*, while in other sites the stain passed between endothelial cells, and did not enter them, for intracellular structures are unstained.

Apparently when venous endothelium is deprived of the blood supply in the vein wall, it may react in two ways. It may desquamate, or some change in permeability to silver nitrate may take place which permits the stain to penetrate it. The suggestion immediately arises that desquamation may be a sequel to some alteration in permeability, allowing fluid to pass through the endothelium and accumulate beneath it, and, thus, lift it off. If this were true, then all endothelium remaining in veins isolated for more than six hours would show subjacent black transverse lines. This does not occur, for in a similar experiment continued for 24 hours and where the endothelium has desquamated in many areas, the clumps of cells which do remain show no black transverse lines beneath them, indicating that desquamation was the principal change rather than some alteration in permeability to silver nitrate (Fig 10).

Where this process is continued for almost the same time, *ie*, 23 hours, in another animal, only a few isolated endothelial cells remain, the surface otherwise showing only the black transverse lines (Fig 11).

If such an experiment is continued for 40 hours, the inner surface of the vein, when examined microscopically, is devoid of endothelial cells, the entire segment being lined by circular muscle fibers (Fig 12). When viewed in cross-section, the endothelium is absent, and the blood in the lumen is seen to be in most intimate contact with the muscular coat of the vein wall. This lumen did contain a small adherent clot.

These specimens, along with many others from similar experiments conducted for varying periods up to 48 hours, indicate that when vein segments are isolated but unobstructed, the first changes that occur (usually in four to six hours) are either focal desquamation or some change in permeability to silver nitrate, and that the desquamation increases as the period of isolation lengthens, becoming complete in some veins in 23 hours.



FIG 10

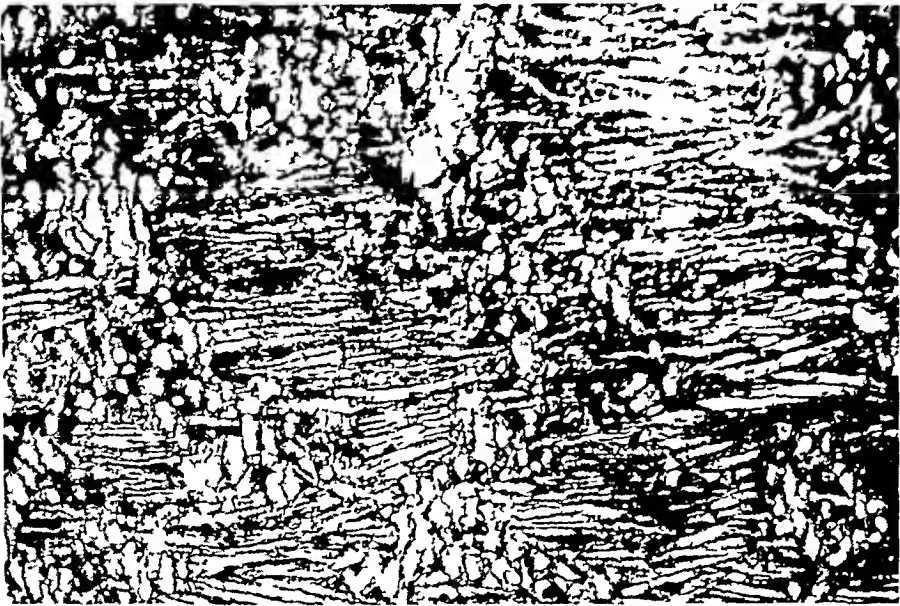


FIG 11

FIG 10—Photomicrograph of endothelium of dog's jugular vein segment after the vein had been isolated for 24 hours from all blood supply to its wall. In areas where the endothelial pattern is absent, the black transverse lines are seen. Many nuclei of endothelial cells appear as relatively light areas. Note that where the endothelial pattern is still present, no transverse lines are visible beneath it.

FIG 11—Photomicrograph of endothelium of dog's jugular vein segment after the vein had been isolated for 23 hours from all blood supply to its walls. Only a few isolated endothelial cells remain, the remaining surface being probably composed of smooth circular muscle. Stained with 0.4 per cent silver nitrate solution ( $\times 210$ ).

FIG 12

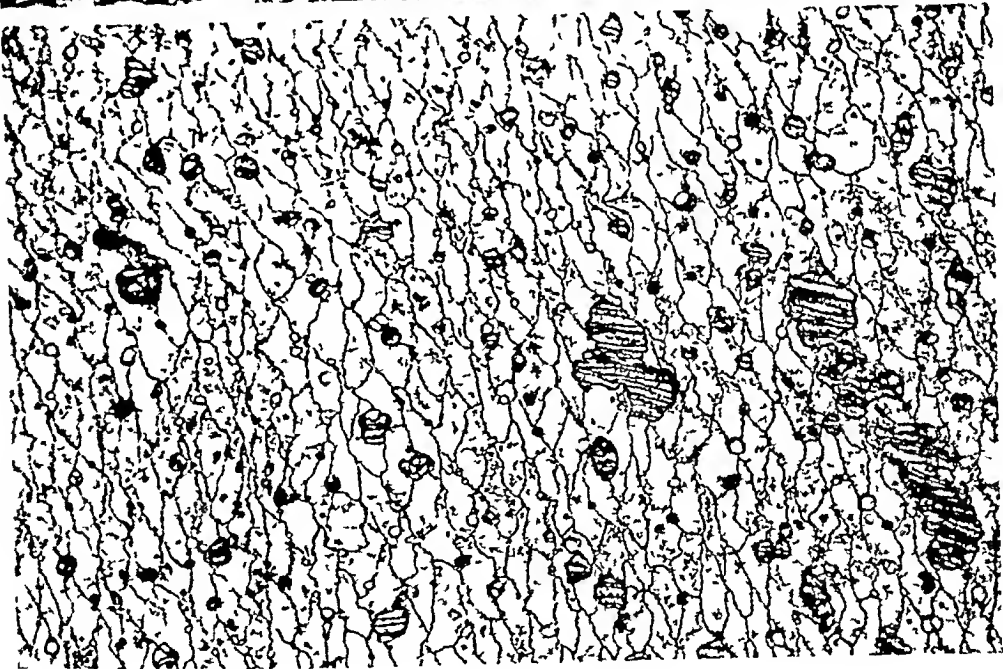
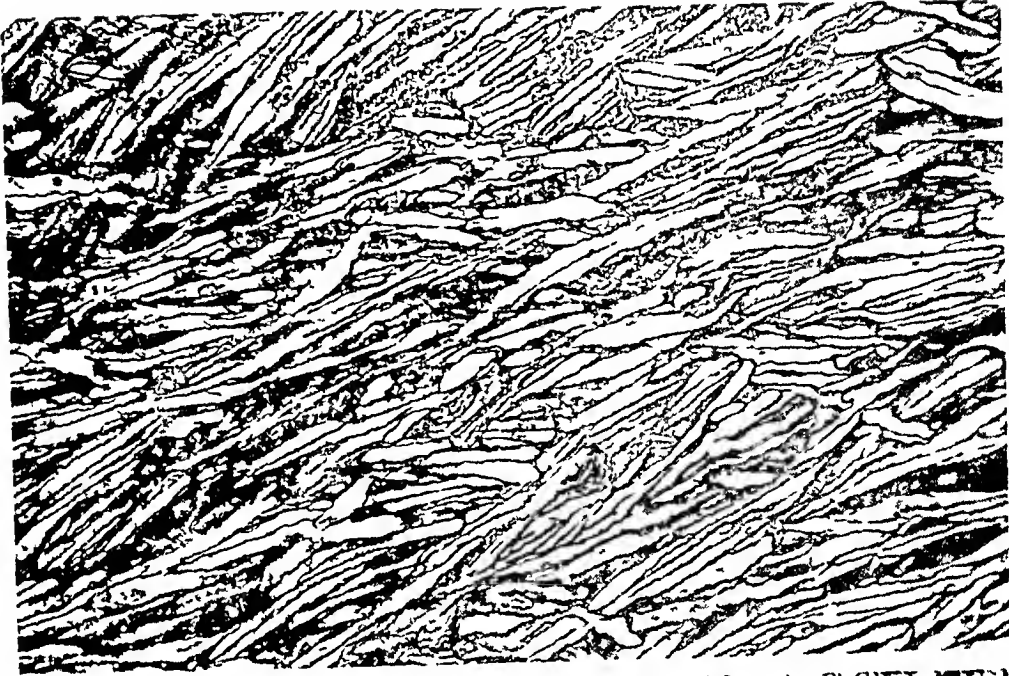


FIG 13

FIG 12—Photomicrograph of endothelium of dog's jugular vein segment after vein had been isolated for 40 hours from all blood supply to its wall. All endothelium has desquamated, leaving a layer of smooth muscle. Stained with 0.4 per cent silver nitrate solution ( $\times 210$ ).

FIG 13—Photomicrograph of endothelium of dog's jugular vein segment after nine hours of partial obstruction of blood flow through the lumen. Stained with 0.4 per cent silver nitrate solution ( $\times 210$ ). The endothelium appears granular, and desquamation is focal.

It is noteworthy that as long as the blood flow in the parent lumen is unobstructed, intravascular clotting seldom occurs, even though endothelial desquamation is maximal. This is strikingly demonstrated by the gross appearance and behavior of these veins after they have lain isolated for over 12 hours. The vein segment under these conditions decreases by as much as 50 to 60 per cent in diameter, probably due to tonic contraction of circular muscle, and the minute volume of blood flow through it is about 25 to 35 per cent of the original. This was determined by placing a wide-mouth, right-angle cannula in the proximal end of each segment before it was removed for mounting and carefully measuring the minute volume outflow and examining it for clots.

Although minute volume of flow was lessened the associated decrease in diameter of the vein helped to maintain the velocity of blood flow at a rapid rate, and it is probably this maintenance of velocity that prevented thrombosis, even in the presence of what are commonly termed "raw" surfaces which in these instances were surfaces lined by muscle, a tissue whose ability to produce thromboplastin has long been respected. These experiments serve to reemphasize the importance of stasis as a factor in the etiology of venous thrombosis.

It can thus, be definitely demonstrated that division of all blood vessels, lymphatics, and nerves to a given segment of vein wall can, over a period exceeding four to six hours, result in increasing degrees of endothelial desquamation.

#### CHANGES IN VENOUS ENDOTHELIUM ASSOCIATED WITH PARTIAL STASIS IN THE PARENT LUMEN

When the experiment is varied so that partial stasis is produced in a vein without severing the vasa venarum, the resulting endothelial changes in the endothelium just distal to the obstruction are similar in type but less marked in severity. Slowing of blood flow was brought about by placing small metal clamps with clearances of 0.75 mm. around the proximal part of a femoral or external jugular vein and permitting them to remain thus for periods ranging from nine to 75 hours. Measurements of minute volume with and without such clamps in place indicate that they reduce blood flow in the parent lumen by 80 to 90 per cent of normal.

When such a clamp remains in place nine hours, and the vein segment distal to it is then removed, stained, and mounted as previously described, the endothelium shows minimal damage (Fig 13), represented by a granular appearance of the endothelium, the presence of an increased number of nuclei and focal endothelial desquamation. A thrombus not attached to the vein wall was present in this vein at the time of removal.

If the slow blood flow is allowed to persist for 29 hours, the endothelium presents minimal to moderate damage (Fig 14). In the flat preparation of vein wall from which the illustration was made, there are very large areas showing no damage, and a few areas wherein the endothelium has desquamated. There was a clot lying free in this vein lumen at the time of removal.

FIG 14

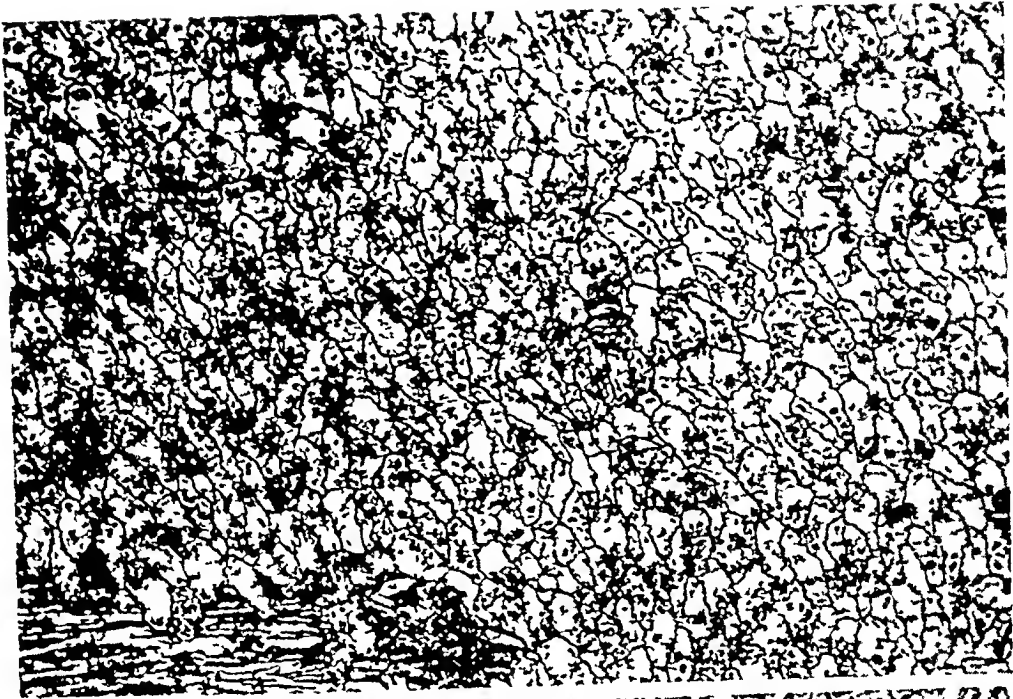


FIG 15

FIG 14—Endothelium of dog's jugular vein after 29 hours of partial obstruction of blood flow in the lumen. Stained with 0.4 per cent silver nitrate ( $\times 210$ ). The endothelium is quite granular, and several areas of desquamation are visible.

FIG 15—Endothelium of dog's jugular vein after 74 hours and 40 minutes of partial obstruction of blood flow in the lumen. Stained with 0.4 per cent silver nitrate ( $\times 210$ ). Transverse lines are visible through the endothelium. Some endothelium has desquamated, and many nuclei are visible.

Experiments conducted in a similar way for 75 hours result in endothelial permeability to silver nitrate in other areas, for the cells are absent in some zones, the nuclei are prominent in other zones, while in still other places black transverse lines can be made out with endothelial cell outlines present above them (Fig 15) There was no clot present in this instance, but the decrease of blood flow was not quite as great as in the two previous veins

In comparing results in the two sets of experiments, namely, isolation of veins without any obstruction, and partial obstruction without isolation, it is justifiable to conclude that isolation without obstruction causes much more endothelial damage, while partial obstruction without isolation, although not as destructive of endothelium, is a slightly more frequent cause of intravenous clotting for the time-periods during which these experiments have been conducted

The objection may occur that, although stasis may well be present, for example, in the lower leg veins of many bedridden patients, there is little reason to feel that circulation through the vasa venarum has been cut off This is true But a variety of disorders may result in decreased oxygen supply to such vein walls To enumerate some of them hypoxia from deep or prolonged anesthesia or narcosis, any interference with pulmonary ventilation, poor oxygen transportation as in some cardiovascular diseases, occlusive arterial disease of extremities, or diminished blood flow to a resting or immobilized limb

Given low oxygen values in arterial blood entering an extremity, both the blood nourishing the walls of the veins as well as the blood returning in the vein lumen may have proportionate decreases in their respective oxygen levels It is conceivable that, under such conditions, venous endothelium is caught in the middle, between two poor oxygen sources whose total supplies are scarcely adequate to keep it intact Add, then, stasis, which means allowing time, and a clot may promptly form Such a theory, which may or may not operate clinically, leads to the proposal that, if it were sound, one should be able to produce venous thrombi consistently in experimental animals either by isolation and partial obstruction of vein segments, or by causing hypoxia plus obstruction of certain vein segments

There is some evidence, as yet not conclusive, that experimental thrombi will regularly result in vein segments from a combination of isolation and partial obstruction of those segments, provided that sufficient time is allowed during which these factors operate In nine experiments so conducted for varying lengths of time, thrombosis occurred in four instances where isolation and partial obstruction were present for more than 24 hours, but in only one instance of five where these conditions existed for less than 24 hours In the animals where thromboses occurred, the experiments were conducted for 24, 25, 30, and 50 hours, respectively Thrombosis occurred once in an experiment of three hours' duration, and not at all in four experiments carried out for 2, 12, 14, and 19 hours, respectively

Much more experience with this approach to the study of vein walls is

required. It is not known whether old animals are more susceptible than younger ones to interference with vasa venarum, and observations so far made regarding this have been very limited due to the difficulty of securing old dogs. Studies will be continued using material obtained clinically where the past history, age, and general condition of the patient can be determined more accurately. Various counterstains will be utilized to permit more accurate interpretation of endothelial changes and to study other physiologic functions of vein walls.

The original suggestion to approach the study of spontaneous venous thrombosis by studying the nutrition of vein walls in flat preparations was made by Dr Cecil K. Drinker. For the opportunity to work on these problems in his laboratory and for his innumerable kindnesses and suggestions, as well as those afforded by his staff—the Misses de Jony, Hardenbergh, Ordway, and Puleo, and Mr Louis Freni—I am deeply grateful.

#### SUMMARY

A new technic is presented for the use of dilute silver nitrate solution in staining and studying the inner coats of vein walls.

A new technic is presented for mounting flat segments of vein walls so that the inner coats of the wall can be stained and studied.

Use of the benzidine stain for outlining the vascular plexus in vein walls is described, and the distribution of these vasa venarum is discussed.

Changes in the inner coats of vein walls following isolation, obstruction, and a combination of isolation and obstruction of vein segments are discussed.

Theoretic connections between anatomy and physiology of vasa venarum, alterations in endothelium, and clinical venous thrombotic lesions are discussed.

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# DUPLICATIONS OF THE ALIMENTARY TRACT\*

## REPORT OF SIX CASES

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DUPLICATIONS are rare developmental anomalies which are found in relation to any portion of the alimentary tract, usually the small intestine. They may be spherical or tubular and vary considerably in size but closely resemble the gastro-intestinal structures, their walls being made up of mucous membrane, smooth muscle and serosa. Duplications are usually discovered in infancy and childhood and they are of clinical importance because of the serious symptoms which they may produce.

Many names have been given to this malformation. In order to simplify the nomenclature, we are in agreement with Ladd<sup>19</sup> and include the terms "enterogenous cyst," "enteric cyst," "inclusion cyst," "ileum duplex," "giant diverticulum" and "unusual Meckel's diverticulum" under the general classification of "duplications of the alimentary tract." Although found in different locations and in different shapes and sizes, they are embryologically associated and should be grouped together. They should not be confused with Meckel's diverticulum, which is an entirely different abnormality with a distinct embryologic derivation.

Six cases of duplication of the gastro-intestinal tract were encountered at Babies Hospital between April, 1945 and November, 1946. All of them came to operation.

## CASE REPORTS

**Case 1**—J. R., a 12-year-old white boy, was admitted to Babies Hospital, April 13, 1945 because of severe bleeding per rectum and weakness. On the morning of admission, he awoke feeling well, went to the bathroom for a bowel movement and passed a considerable quantity of fresh blood with his stool. He called to his mother and fainted. Four hours later he was brought to the hospital. There had been no previous episode of gastro-intestinal bleeding. The personal and family histories were noncontributory.

Examination on admission revealed a pale, apprehensive child with cold, clammy extremities. The pulse was 84, respirations 30, temperature 98.6° F and blood pressure 94/40. The other physical findings were normal except for the presence of fresh blood in the rectum. A transfusion of 500 cc. of whole blood was administered, and proctoscopic examination performed one hour after admission. No abnormality was found, but fresh blood was seen coming from above the tip of the proctoscope. After the transfusion, the hemoglobin was 10.2 Gm. and the red blood cells 3,720,000. The leukocyte count was 11,000, with 68 per cent polymorphonuclear cells, 30 per cent lymphocytes and 2 per cent eosinophils.

During the ensuing four days he improved, there was no gross bleeding but the stools remained tarry and gave 4-plus reactions to the guaiac test. He was asymptomatic and maintained his hemoglobin and red blood count at about the same levels. On the 5th

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hospital day, roentgenologic examination of the colon by means of a barium enema was done and no abnormalities were demonstrated. The barium was returned containing gross blood. The hemoglobin dropped to 7.2 Gm (48 per cent) about seven hours later and he received another transfusion of 500 cc of whole blood. After the 11th hospital day the stools became normal, and roentgenographic study of the gastro-intestinal tract was carried out after barium meal. Nothing abnormal was demonstrated.

*Operation*—Celiotomy was performed, May 9, 1945, under ether anesthesia. The pre-operative diagnosis was Meckel's diverticulum, with ulceration and hemorrhage. About 15 cm proximal to the cecum a small duplication of the ileum was found. It projected from the mesenteric side of the bowel, measured 3 × 2 × 2 cm and extended out between the leaves of the mesentery plate (Plate IA). A segment of bowel containing the duplication, and extending 2 cm above and below it, was resected. The patient made an uneventful recovery, and was discharged on his 14th postoperative day.

*Follow-up*—A few months after operation he received radiotherapy for keloid formation in the scar. When last seen, November 22, 1946, 18 months postoperatively, he was asymptomatic.

*Pathology*—The specimen consisted of a segment of ileum measuring 7 cm in length. From the midportion projected an ovoid, soft, pale yellow structure 3 × 2 cm (Plate IA). It was attached by a broad base, 2 cm in diameter, to the mesenteric side of the bowel. On section (Plate IB), the cavity of the duplication was shallow and the lateral walls resembled intestinal mucosa. The mucosa was pale and spongy.

Microscopically (Fig 1), portions of the internal surface were covered by intestinal mucosa as evidenced by villi and intestinal glands containing Paneth cells. Contiguous to the intestinal mucosa there were areas where the surface was lined by tall columnar, eosinophilic epithelial cells, and deeper in the mucosa there were many gastric glands. In some regions parietal cells predominated. A few clusters of Brunner's glands were also present. In one part, there was a deep ulcer. Its base was covered by eosinophilic material and the wall, including muscularis, was entirely replaced by granulation tissue which extended into the submucosa and serosa of the bowel lateral to the ulcer.

**Case 2**—P. K., a 35-months-old white male, was admitted to Babies Hospital, December 21, 1945 with a history of pallor and tarry stools of five weeks' duration. At the age of two months he first passed a small amount of fresh blood per rectum. Subsequently, the stools became tarry and remained so until admission. At the age of three months a gastro-intestinal roentgen series and a barium enema, done at another hospital, were reported as normal.

## PLATE I

A—Case 1 Duplication of ileum protruding from mesenteric side

B—Case 1 Inner aspect of duplication showing hyperplastic gastric mucosa which forms a contrast to the normal intestinal mucosa of the ileum

C—Case 2 The orifice by which the duplication communicates with the ileum is indicated by scissors and lies at the lower (distal) end of the accessory bowel. The duplication runs proximally along the mesenteric side of the ileum, between the leaves of the mesentery, for a distance of 10 cm and then lies free. The dilated middle portion is lined with gastric and small intestinal mucosa and an ulcer is visible. The rounded enlargements near the free extremity are lined with gastric mucosa, while the mucosa of the narrow portion between them was found to resemble common bile duct mucosa.

D—Case 4 A duplication lined with gastric mucosa. The external fistula is shown in the upper left corner of the specimen.

E—Case 5 The duplication lies within the mesentery in close approximation to the ileum.

F—Case 6 The duplication lies within the mesentery in apposition to the normal intestine and communicates with it at the lower end.

G—Case 6 The mucosa of the duplication bears thick irregular folds resembling gastric mucosa. That of the small intestine bears transverse folds suggesting the valvulae conniventes of jejunum, as in Case 2, Plate IC.

A



B



G



Except for marked pallor the physical findings were within normal limits on admission. The hemoglobin was 6 Gm, and the red blood cells 2,760,000. The leukocyte count was 6,100, with 48 per cent polymorphonuclear cells, 50 per cent lymphocytes and 2 per cent monocytes. The platelet count, the bleeding and coagulation times were normal. The stools were tarry and gave a 4-plus reaction to the guaiac test. No abnormalities were found on proctoscopic examination. He was given small transfusions of whole blood in preparation for surgery.

*Operation*—On the 5th hospital day, celiotomy was performed under ether anesthesia. The preoperative diagnosis was Meckel's diverticulum, with ulceration and hemorrhage.

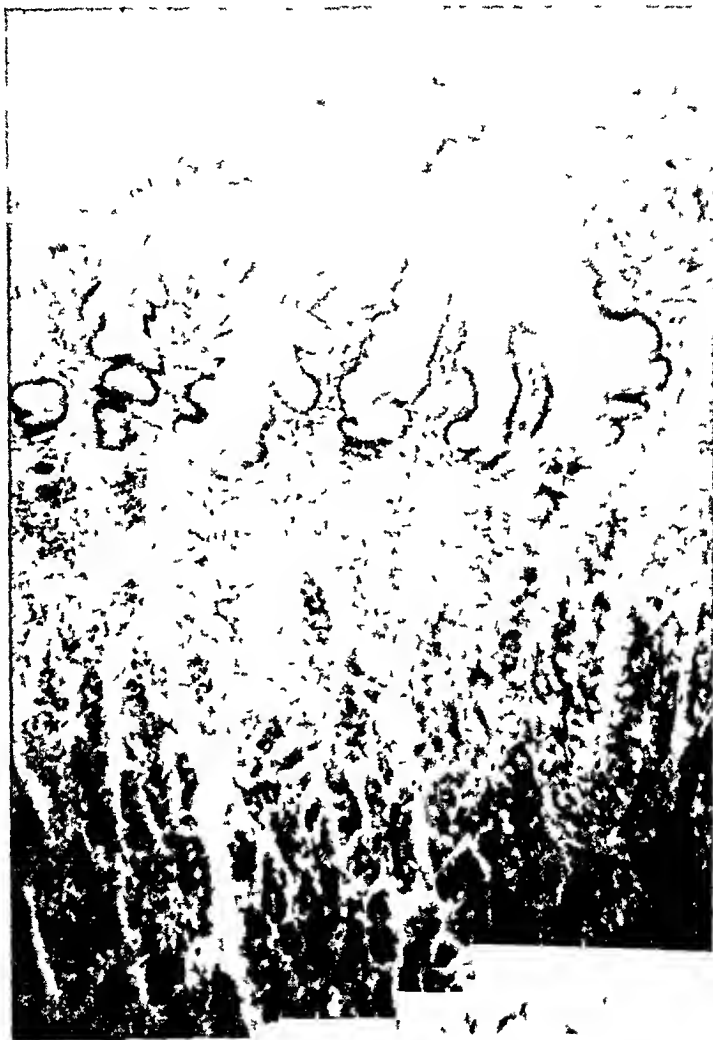


FIG 1—Case 1 Hyperplastic gastric mucosa lining the duplication

About 20 cm proximal to the ileocecal area a duplication of the bowel was found (Plate IC). Starting at the distal end and following it backward, we found that the duplicate intestine was attached to the ileum and coursed proximally along its mesenteric side for 10 cm. It then deviated from the normal bowel and continued separately for a total distance of 22 cm, cephalad and posteriorly, along the mesentery to the region of the pancreas. After its separation from the normal bowel, the duplication resembled small intestine for about 10 cm. A dilated segment was then met, measuring 6 cm in length. This portion contained blood and an ulcer was palpable on the posterior wall. Beyond this there was a narrow empty segment, 25 cm in length, followed by a rounded enlargement, 15 cm in diameter. There then was another narrow segment, 1 cm

in length, and the final portion, or the proximal extremity of the duplication, was a slightly enlarged blind end about 1 cm in diameter

Dissection was started at the proximal or free end of the duplication and mobilization was possible without interfering with the blood supply to the normal bowel. This was carried out down to the point where the accessory intestine fused with the normal ileum. Here, the mesenteric vessels were common to both duplication and normal bowel. This part of the anomaly was then resected together with the contiguous normal ileum and a side-to-side anastomosis performed. Convalescence was uneventful, and the patient was discharged on the 14th postoperative day.

Follow-up—When last seen, November 22, 1946, 11 months after operation, he was developing normally, his nutrition was excellent and there were no symptoms referable to the alimentary tract.



FIG 2—Case 2. Section through the chronic ulcer in the dilated middle portion of the duplication. The margin of the ulcer is formed by ileum. Gastric mucosa, which is not shown, is nearby.

*Pathology*—The gross external findings were essentially the same as described in the operative note above. On section (Plate IC), the orifice by which the duplication communicated with the ileum was found at the lower (distal) end of the accessory intestine. The mucosa of the lower portion of the duplicate bowel (that part which paralleled the normal ileum and extended to the dilated segment) resembled jejunum and the lumen contained thin watery fecal material. The mucosa of the dilated midportion was thick, and resembled gastric mucosa. It bore a rather deep ulcer, 1.5 cm in diameter, with thickened margins and a bed of fibrous tissue. The mucosa of the two rounded enlargements at the upper end was thick and infolded, and also resembled gastric mucosa. The mucosa of the two narrow areas was thin and smooth.

Microscopically, one section through the lower or distal half of the duplication showed mucosa resembling that of the colon and bore a small ulcer extending into the submucosa. A second section through the lower end of the duplication showed gastric mucosa.

A section through the ulcer in the dilated part of the accessory bowel (Fig 2) showed small intestinal mucosa on both sides of the ulcer. On one side, however, slightly beyond the intestinal mucosa, there was an abrupt transition to well-differentiated gastric

mucosa The ulcer extended to the level of the muscularis, and beneath this there was a thick wall of fibrous tissue containing many fibroblasts and young fibrocytes The underlying peritoneum was thickened with fibrous tissue and covered with a delicate layer of fibrin A few lymphocytes, plasma cells and phagocytes infiltrated the entire scarred area, and there was fresh hemorrhage into the deeper portion

Sections through both nodular enlargements of the free end of the duplication showed gastric mucosa infiltrated with a few eosinophils

A section through the narrow segment connecting the two nodular enlargements was



FIG 3—Case 2 Section through the narrow portion near the free end of the duplication in which the mucosa resembles that lining the common bile duct

lined with a thin and irregular layer of high columnar cells which suggested the structure of common bile duct mucosa (Fig 3)

The mucosa of the resected normal small intestine was edematous and bore transverse folds as in jejunum A few Paneth cells were present and also a cluster of three lymph follicles It was not clear whether the mucosa was that of jejunum or ileum

Case 3—J H, a five-year-old white boy, was admitted to Babies Hospital, February 25, 1946, because of abdominal pain and vomiting of six days' duration The pain was intermittent and confined to the lower abdomen Vomiting followed the onset of pain and had occurred about twice daily The stools were normal until the day of admission, when they became liquid, and contained some small blood clots

On admission, the physical findings were within normal limits except for minimal tenderness and rigidity over the right lower quadrant of the abdomen. The temperature was 100.4 F, pulse 88, respirations 22. The leukocyte count was 18,400, with 77 per cent polymorphonuclear cells and 23 per cent lymphocytes. The red blood count and urine analysis were normal. The sedimentation rate was 19 mm in one hour. The stools gave a 4-plus reaction to the guaiac test. No pathogens were recovered from stool culture. The Kline test was negative.

The next day, the leukocyte count was 10,600, with 68 per cent polymorphonuclear cells and 32 per cent lymphocytes. Physical findings were the same. On the 4th hospital day, roentgen study of the colon by means of a barium enema disclosed no abnormality. The patient remained asymptomatic for the next three days.

On the 7th hospital day, shortly after breakfast, he suddenly complained of lower abdominal pain. He was not nauseated, and did not vomit. There was moderate tenderness over the lower abdomen, slightly more on the right than the left, but no rigidity. Rectal examination was normal. He had a normal bowel movement one hour later. The temperature was normal. The leukocyte count was 16,200, with 88 per cent polymorphonuclear cells. By the afternoon, eight hours after the onset of pain, he was asymptomatic and physical findings were normal. The next day, the leukocyte count was 10,000, with 65 per cent polymorphonuclear cells. Two days after this episode, he was again seized with severe pain in the left upper quadrant, which soon shifted to the lower abdomen, and was accompanied by nausea and vomiting. At this time, there was marked tenderness and rigidity of the entire lower abdomen.

*Operation*—Celiotomy was performed, and a small duplication of the ileum was found 30 cm proximal to the ileocecal area. It measured 3 × 2 × 2 cm, and extended out between the leaves of the mesentery. (We do not have a photograph of this specimen but it closely resembled that found in Case 1 (Plate IA).) About 200 cc of serosanguineous fluid were present in the peritoneal cavity. The terminal ileum was edematous and thickened. The duplication and about 10 cm of ileum above and below it were "peppered" with areas of subserosal hemorrhage. The mesentery and its nodes in this region were thickened and edematous. It seemed probable that the duplication had produced an intussusception, which had reduced spontaneously just before operation. In all, 24 cm of the ileum together with the duplication were resected and a primary anastomosis performed. Convalescence was uneventful, and the patient was discharged on the 10th postoperative day.

*Follow-up*—This patient was last seen on November 22, 1946, nine months after operation, when he was asymptomatic.

*Pathology*—The gross external findings were as described above. In a section through the duplication, the mucosa showed transverse folds and resembled duodenum. The mucosa and part of the submucosa were densely packed with polymorphonuclear cells, phagocytes and red blood cells. Some of the superficial portions of the villi had lost their epithelium. Most of the muscle cells showed early necrosis. The peritoneum was hemorrhagic. The section suggested early gangrene. A section through the adjacent ileum showed edema and infiltration of the mucosa with polymorphonuclear cells. Sections taken farther away from the duplication were normal.

*Case 4*—B. M., a ten-months-old white male, was admitted to Babies Hospital, February 22, 1946, with a fistula in the right upper abdominal quadrant. At the age of three weeks this patient was said to have a small, red, tender mass in the right upper quadrant. Two months later, when the mass had increased to the "size of a plum," he was admitted to another hospital where a diagnosis of abdominal wall abscess was made. The mass was incised but no pus was found, only "edema and thickening of the abdominal wall." Two weeks later he was admitted to the same hospital with the same mass and a fistula at the site of incision. The fistulous tract was excised. One week after this operation, "intestinal fluid" began to drain from the incision, which failed to heal. Four months later another unsuccessful attempt was made to excise the fistula, and the wound

continued to drain. He received nine blood transfusions during his period of hospitalization. Roentgenographic studies of the gastro-intestinal tract, both with barium meal and barium enema, were reported to be normal, as was also an intravenous pyelogram. At the age of ten months, the patient was transferred to Babies Hospital.

On admission, examination revealed a very alert, marasmic infant, who was in no acute distress (Fig. 4). The abdomen was distended but soft and presented a large



FIG. 4—Case 4. Photograph on admission. A dressing soaked with sodium bicarbonate solution is seen in the large fistula.

fistula in the right upper quadrant. The ulceration was about 4 cm. in diameter and about 2 cm. in its deepest portion. It was surrounded by a large area of excoriation and induration. The fistula drained a copious amount of seromucoid fluid. The red blood count and hemoglobin were normal. The leukocyte count was 19,800, with 54 per cent polymorphonuclear cells. The urine analysis was normal. The serum proteins were 6.05 Gm. per 100 cc., with 4.01 Gm. of albumin and 2.04 Gm. of globulin. The plasma chloride



level was 105 milliequivalents per liter. The stools gave a negative reaction to the guaiac test. Roentgenographic studies, with lipiodol injected into the fistula, failed to demonstrate any connection with the alimentary tract. Visualization of the gastro-intestinal tract with barium showed the second portion of the duodenum displaced to the left, suggesting a mass impinging on its descending limb from the right. There was no evidence of obstruction.

Methylene blue fed by mouth failed to appear in the fistula. In an histamine test, the fluid flowing from the fistula was collected quantitatively, as if for gastric analysis, with the following results. The free HCl before histamine was zero, the total acidity 70. After histamine, the free HCl was 38.5, the total acidity 79, and the amount of drainage was considerably increased. By direct measurement, the pH of this fluid was 3.0. Pancreatic enzyme assay performed on the fluid showed no trypsin or amylase. The fistulous tract was continuously treated with dressings of sodium bicarbonate solution, and the surrounding skin slowly began to improve. The discharge was so irritating to the skin that at one time, when the dressings were neglected overnight, a red tract of excoriated skin was seen the next morning where the fluid had run down the flank.

After four weeks of supportive therapy the skin around the fistula had improved sufficiently to permit operation. From the evidence gathered, we expected to find a duplication of the stomach, probably devoid of direct communication with the alimentary tract.

*Operation*—Celiotomy was performed, under ether anesthesia, March 26, 1946. The patient received 200 cc of whole blood during the procedure. A subcostal incision, just above the fistula, was made. Because of the dense adhesions encountered, the lateral end of the incision was extended downward and medially below the fistula in order to secure adequate exposure. The fistulous tract led into a cystic mass which was round, thick-walled, and grossly resembled stomach. The mass lay in the gastrohepatic omentum and was in contact with the edge of the liver and fundus of the gallbladder anteriorly and the transverse colon posteriorly and inferiorly. The stomach was normal. A loop of jejunum was adherent to the point where the fistulous tract joined this mass and communicated with the tract through a minute opening. This was interpreted as a traumatic fistula probably resulting from one of the previous operations. The mass itself, however, had no direct communication with any of the viscera.

The adherent loop of jejunum was dissected free of the fistulous tract and the small opening in it was closed. The duplication was then dissected free from the surrounding structures and was removed together with the fistulous tract. The incision was closed in layers, and the fistulous opening remaining in the abdominal wall was packed with gauze.

This opening soon filled-in with granulation tissue and became covered with epithelium. A small segment of skin in the lower extension of the incision sloughed because of poor blood supply, and this defect was allowed to heal by granulation.

Six weeks postoperatively the patient developed mumps, and was transferred to the Willard Parker Hospital. He was readmitted to Babies Hospital one week later for further care of his wound. He was discharged on June 15, 1946, when the wound was entirely healed.

*Follow-up*—He was last seen, October 25, 1946, seven months after operation. He had gained a great deal of weight and was developing normally. There were no symptoms referable to the gastro-intestinal tract. The wound was well-healed but presented some weakness at the lateral end of the subcostal scar.

*Pathology*—The specimen (Plate ID) consisted of a rounded mass measuring 3.3 x 2.8 x 2.2 cm. It bore two short projections: one measured 1 cm in diameter and 0.5 cm in length and was patent, the other was a tag of fibrous tissue 1 cm in length. On section, the cystic mass contained 5 cc of thick, cloudy, brownish-black fluid. The inner surface resembled gastric mucosa. No ulcers were seen. The wall measured 5–6 mm and was formed of a mucosal and a muscular layer of about equal thickness.

The microscopic sections resembled hyperplastic stomach wall. The mucosa was thick and the chief cells were clearly seen. No ulcer was present. The muscularis was in two layers with distinct sympathetic ganglia between them. The muscle fibers were hypertrophied. The peritoneum was somewhat edematous.

**Case 5**—J. B., a three-months-old white male, was admitted to Babies Hospital, May 7, 1946, because of bleeding per rectum. The baby was well until three weeks previously, when the mother noted fresh blood on his diaper. The next day he passed blood clots by rectum, following which he began to look pale. The hemoglobin was reported to be 40 per cent, and he was admitted to another hospital for transfusions and surgery. At operation, a duplication of the ileum was found. No resection was attempted because of his poor condition. In the first days after exploration, he had eight bloody stools, received two blood transfusions, and then gradually began to show improvement. Two weeks after operation he had an "alarming rectal hemorrhage," was given another transfusion of whole blood and transferred to Babies Hospital.

On admission, the infant was very pale and listless. The abdomen was soft and showed a healed right rectus incision. No masses were palpable. Gross blood was found in the rectum on digital examination. The hemoglobin was 9 Gm., the red blood cells 3,700,000. The leukocyte count was 16,000, with 45 per cent polymorphonuclear cells and 55 per cent lymphocytes.

After a transfusion of 100 cc. of whole blood the hemoglobin rose to 11.7 Gm. and the red blood cells to 4,300,000. He continued to pass small quantities of gross blood by rectum.

**Operation**—On the 3rd hospital day operation was performed under ether anesthesia. About 25 cm. proximal to the ileocecal region, a duplication was found which measured 15 cm. in length (Plate IE). The duplication and the contiguous ileum were resected.

Convalescence was uneventful and the patient was discharged on the 13th postoperative day.

**Follow-up**—He was last seen, November 26, 1946, six months after operation, he was asymptomatic, and no further bleeding had been observed.

**Pathology**—The specimen (Plate IE) consisted of a segment of ileum measuring 20.5 cm. in length and 1.3–1.5 cm. in diameter. Running parallel to it, on the mesenteric side, and enclosed in the same peritoneal sheath, there was a duplicate segment of intestine measuring 15.5 cm. in length and 1.8–2.2 cm. in diameter. The junction of the two, near the distal end of the specimen, extended for a distance of about 3 cm. The mucosal surface of the ileum looked normal except for the presence of the orifice into the accessory intestine. This appeared as a transverse slit 1.2 cm. in width. The mucosa of the duplication was thick and somewhat irregular, resembling that of the stomach. The transition to ileal mucosa was abrupt and followed a transverse line just proximal to the communication.

Microscopically, the sections showed a portion of ileum which made an abrupt transition to hypertrophic gastric wall. The gastric mucosa was very much infolded. The deeper layer contained normal gastric glands with numerous chief cells. The stroma was infiltrated with a moderate number of lymphocytes. The muscularis was normal and the peritoneum was thick and edematous.

**Case 6**—R. N., a six-year-old white boy, was last admitted to Babies Hospital, November 10, 1946, with a history of abdominal pain and bleeding per rectum. His illness began at the age of three months, when the parents first noticed that his stools were tarry. This condition was only temporary. When he was seven months old he passed two large bloody stools for which he was admitted to another hospital and received two blood transfusions. Roentgenographic studies were made of the gastrointestinal tract, including barium enema. These were reported to be normal and he was discharged after eight weeks of observation.

He was first admitted to Babies Hospital in 1942, at the age of 15 months, because he had again passed gross blood by rectum. The hemoglobin was 5.1 Gm. (35 per cent),

and the red blood cells 2,200,000. He received two transfusions. Proctoscopic examination did not reveal any abnormality.

On the 10th hospital day celiotomy was performed. The preoperative diagnosis was Meckel's diverticulum, with hemorrhage. A duplication of the distal ileum was found which was estimated to be 24 inches long. There was an inflammatory mass in the mid-portion of the lower abdomen involving the tip of the appendix, the proximal end of the duplication and a loop of ileum. There was a fistula between this loop of ileum and the duplication. The adherent loop of ileum was dissected free of the mass and the openings in this loop and in the duplication were closed. The appendix was mobilized and removed. Three ulcers were palpated in the duplication. Since the condition of the patient did not justify an extensive resection, the ulcers were inverted with purse-string sutures and the abdomen closed. Convalescence was uneventful. He was discharged, and was to return at a later date for resection of the lesion.

Two months later, at the age of 17 months, he was readmitted because of intermittent abdominal pain and tarry stools. The hemoglobin was 3.8 Gm., and the red blood cells 2,000,000. The parents refused to allow a second operation at this time, and he was discharged after receiving two more blood transfusions.

This patient had seven more admissions to Babies Hospital between the ages of 18 months and four years, each time for abdominal pain, tarry stools and anemia. On each occasion, permission for operation could not be obtained, and he was discharged after receiving transfusions of whole blood. Between the ages of four and six years there were no further episodes of bleeding.

Two days before the most recent admission, he was awakened by severe abdominal pain at 4 A.M., and soon vomited. He ate breakfast at 7 A.M., and vomited again after an attack of violent lower abdominal pain which doubled him up and caused him to roll on the floor. Following this episode, the pain disappeared and the next day fresh blood was noticed in his stools.

Except for marked pallor, the physical findings were within normal limits on admission. The hemoglobin was 5.5 Gm., and the red blood cells 2,320,000. The stools were tarry and gave a 4-plus reaction to the guaiac test. This time permission for operation was granted and he received three transfusions of whole blood in preparation for surgery.

*Operation*—On the 9th hospital day celiotomy was performed under ether anesthesia. Many adhesions were encountered between the duplication and loops of small intestine. The distal end of the duplication, where it communicated with the normal bowel, was found about 40 cm. proximal to the ileocecal area. It coursed upward along the mesenteric side of the ileum for a total length of 40 cm. (Plate IF). At its proximal extremity it deviated from the normal ileum and ended in a blind pouch between the leaves of the mesentery. The duplicate intestine, together with 60 cm. of the contiguous ileum, were resected.

Postoperatively, he did well except for an episode of abdominal cramps and vomiting on the 8th day which promptly responded to the use of the Miller-Abbott tube. He was discharged on the 20th postoperative day in excellent condition.

*Follow-up*—This patient was last seen, January 27, 1947, ten weeks after operation. He was having normal bowel movements and there had been no further episodes of pain since discharge. He was gaining weight rapidly, an estimated ten pounds since operation.

*Pathology*—The specimen (Plate IF) consisted of a loop of small intestine measuring 60 cm. in length and 2 cm. in diameter. A second segment of bowel lay parallel to it on the mesenteric side and within the mesentery, sharing a common blood supply. This measured 40 cm. in length and 2–2.5 cm. in diameter. The duplicate portion communicated freely with the normal intestine at the lower end of the specimen. The proximal end formed a somewhat dilated blind pouch, 4 cm. in diameter. This was demarcated from the remainder of the duplication by a slight constriction 4 cm. from the extremity. The main portion of the duplication measured 5 cm. in circumference. The lumen was filled with dark, brownish-black mucoid material. The mucosa (Plate IG)

was thick and grey, and thrown up into irregular folds, the appearance being that of gastric mucosa. The ulcers described at the previous operation, 45 years ago, were not evident. The mucosa of the small intestine was yellowish and bore transverse folds similar to those of the normal jejunum.

Microscopically, the duplication showed normal gastric mucosa diffusely infiltrated with lymphocytes and eosinophils (Fig 5). No ulcers were present. The submucosa was normal. The circular and longitudinal muscular layers were of approximately equal thickness throughout. They were infiltrated with a few eosinophils. Sections through the contiguous small intestine showed transverse folds similar to those of jejunum. Paneth cells were absent and no Peyer's patches were present. It was not clear whether the mucosa was that of jejunum or ileum.

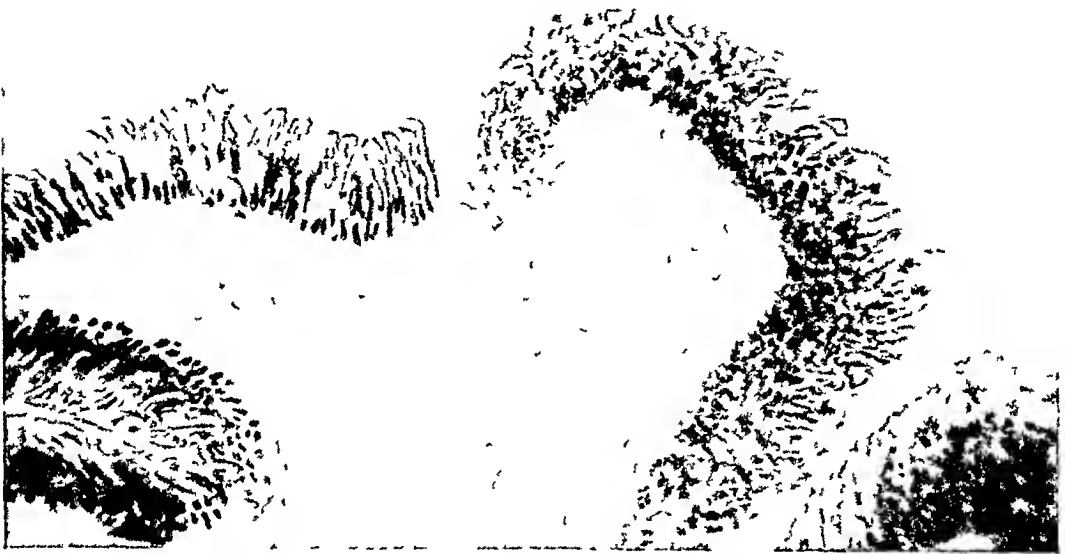


FIG 5—Case 6. The section is taken from the junction of the duplication with the intestine. The transition between the gastric and intestinal mucosa is abrupt. The fusion of the muscular coats of the two portions of bowel is demonstrated.

#### DISCUSSION

*Embryology*—There are many theories regarding the origin of duplications. According to Hughes-Jones,<sup>15</sup> the sequestration of embryonal intestinal epithelium early in fetal life may account for the development of these anomalies. Many authors have previously described these cases as representing persistence of the proximal part of the vitelline duct or Meckel's diverticulum. As pointed out by Hudson,<sup>14</sup> the persistence of the vitelline duct, a normal fetal structure, explains many cysts and diverticula but this accounts only for those which occur in relation to the distal portion of the ileum. Also, this theory would not account for the mesenteric position of the duplications as in contrast to the constant antimesenteric location of Meckel's diverticulum. The case reported by Grove and Porch,<sup>12</sup> of a duplication of the terminal ileum associated with a Meckel's diverticulum and an intramesenteric diverticulum in the same patient, would be difficult to explain on this basis.

Probably the most popular theory of their development is that of Lewis and Thyng,<sup>22</sup> who described groups of epithelial cells or diverticular occurring along the alimentary tract of the embryos of the pig, rabbit, cat, sheep and man, which normally disappear. One of these diverticula may be pinched-off and develop into a duplication.

More recently, Bremer<sup>4</sup> divided these anomalies into two groups, the spherical and the tubular, on the basis of embryologic origin. Most of the spherical ones are derived from true diverticula which are frequently found projecting from the antimesenteric surface of the alimentary tube in embryos of the 8th or 9th week. These diverticula normally regress. Abnormally, they continue to grow and give rise to the spherical type of duplication. Most of the tubular structures, and a few of the spherical ones, represent true duplications, originating by an abnormal persistence of the vacuoles which are regularly present in the "solid stage" of the development of the intestine in the 6th or 7th week embryo. By the confluence of a chain of these vacuoles a new channel is formed alongside the original lumen and this develops as a duplication.

*Pathology*—Duplications may occur anywhere along the gastro-intestinal tract, from the base of the tongue to the rectum. They are most commonly found along the ileum: seven out of the 18 cases reported by Ladd and Gross,<sup>20</sup> five of our six. These lesions may also be found in the mediastinum, as reported by Mixter and Clifford,<sup>24</sup> and others.

The duplicate intestine is usually intimately associated with the normal adjacent bowel, lying on its mesenteric side, between the leaves of the mesentery. The blood supply of the duplication and that of the contiguous intestine are the same. This is of primary importance in the surgical management of these lesions and will be given greater consideration later. Rarely, the malformation may be entirely separate from the alimentary tract, as in one of our cases (Case 4), and is then commonly referred to as an enteric or enterogenous cyst.

These structures may be spherical or tubular. They may vary considerably in size, from 2 cm. to 40 cm. in our cases. Hudson<sup>14</sup> reported one of the ileum about four feet long. They may be multiple, as in the case reported by Poncher and Milles.<sup>26</sup>

The duplication may communicate with the adjacent intestine at one or more points, or not at all. Only two of the 18 cases reported by Ladd and Gross<sup>20</sup> had such an opening. Five of our six cases communicated with the normal bowel. From a study of our cases and a partial survey of the literature, it seems that in the elongated type the duplication usually communicates with the contiguous normal intestine near its distal portion and ends blindly in the mesentery in its proximal portion.

The structure of the duplication is essentially that of the gastro-intestinal tract, the wall being made up of mucosa, smooth muscle and serosa. The mucous membrane is not necessarily the same as that of the adjacent segment of intestine. In three of our cases it was entirely gastric, in one it was gastric

and small intestinal, in one it was duodenal and in one it was mixed, containing gastric, small intestinal, colonic and common bile duct mucosa

The occurrence of ectopic gastric mucosa is often associated with ulcers and bleeding. However, bleeding may occur with apparently intact mucous membrane (Cases 5 and 6). Acute perforation has been reported by Black and Benjamin.<sup>7</sup> Perforation of an ulcer, with the formation of a fistula into the small intestine, probably occurred early in the disease in one of our cases (Case 6).

It is curious that in two of our cases (Cases 2 and 6), the resected normal intestine resembled jejunum more than ileum on pathologic examination although the external appearance and relations, as seen at operation, were definitely those of ileum. We have no explanation for this observation nor have we found any reference to it in the literature.

*Clinical Findings*—The incidence of this condition is difficult to determine. Certainly, it is rare. The fact that we operated upon six cases in a period of 18 months, and that they are being more frequently reported by others, leads us to believe that these abnormalities may not be as rare as previously supposed.

Duplications are usually found in infancy and childhood, but they have been reported in older patients.<sup>7, 9, 23</sup> Our youngest patient was three months old at operation, the oldest was 12 years.

Most of the duplications are found in males, there being only an occasional case reported in females. All of our patients were boys. It is of interest to note that 85 per cent of the reported cases of Meckel's diverticulum are in males,<sup>10</sup> and almost all those associated with bleeding are in the same sex.<sup>1</sup>

There are no characteristic symptoms caused by this anomaly, and a correct diagnosis is rarely made before operation. It may not cause any symptoms and may be discovered as an incidental finding at autopsy. However, it frequently causes serious symptoms. In four of our cases, severe intestinal hemorrhage was the first sign (Table I). Intermittent abdominal pain may be a feature, as in two of the cases. In one of these it was probably due to intussusception of the duplication (Case 3). Palpation of an abdominal mass is a common finding in the series reported by Ladd and Gross.<sup>20</sup> One of our most unusual cases (Case 4) presented a fistula which followed incision of a palpable abdominal mass at another hospital. In none of our other cases was the duplication palpated preoperatively. The anomaly may lead to intestinal obstruction by encroaching on the adjacent bowel, by taking part in a volvulus as in one of Hudson's<sup>14</sup> cases, or by forming the leading point of an intussusception, as in a case reported by Ladd and Gross,<sup>20</sup> and one presented by Kimpton and Crane.<sup>16</sup> There may be severe anemia in the bleeding cases. Malnutrition may be an important part of the picture in some instances.

Roentgenologic findings are not characteristic. The diagnosis is only rarely suggested by displacement of the normal bowel by an abnormally situated air-containing viscus. The duplication is not outlined by barium.

In the differential diagnosis, Meckel's diverticulum, intestinal polypus,

mesenteric cyst, urogenital cyst, dermoid or teratoma, hydatid cysts and pancreatic cysts are to be considered. Meckel's diverticulum with hemorrhage was the preoperative diagnosis in four of our cases. With this experience, we now think of duplication as frequently as we do of Meckel's diverticulum in cases of intestinal hemorrhage.

*Treatment*—The treatment in all instances is surgical and should consist of resection or excision of the anomaly. In the majority of cases, the duplication is intimately attached to the contiguous bowel and separation is impossible without entering the lumen. Furthermore, the blood supply is usually common to both the duplication and the adjacent intestine. The malformation lies between the leaves of the mesentery with the mesenteric vessels coursing over it, anteriorly and posteriorly, and then supplying the contiguous normal bowel distally. For these reasons, resection of the duplication alone is usually impossible and resection of the adjacent bowel is also necessary. This was done in five of our cases. Rarely, the duplication is entirely separate from the alimentary tract and may be excised alone without compromising the blood supply to adjacent structures. This was accomplished in one of our cases.

TABLE I  
DUPLICATIONS OF THE ALIMENTARY TRACT\*

No.	Age	Presenting Symptoms	Location and Size	Type of Mucosa	Treatment
1	12 yrs	Bleeding	Terminal ileum 3 x 2 x 2 cm	Gastric and small intestinal	Resection and anastomosis
2	3 mos	Bleeding	Terminal ileum 32 cm long	Gastric colonic common bile duct small intestinal (jejunal?)	Resection and anastomosis
3	5 yrs	Pain and bleeding	Terminal ileum 3 x 2 x 2 cm	Duodenal	Resection and anastomosis
4	10 mos	Mass and fistula	Gastrohepatic omentum 3.3 cm in diam	Gastric	Excision
5	3 mos	Bleeding	Terminal ileum 15.5 cm long	Gastric	Resection and anastomosis
6	6 yrs	Bleeding and pain	Terminal ileum 40 cm long	Gastric	Resection and anastomosis

\* Table of Cases listed in their chronologic order of operation and corresponding to the Case numbers in the text.

All patients made an excellent recovery.

Operations of lesser magnitude, such as marsupialization of the duplication, with subsequent destruction of its mucosa, or the procedure presented by Gardner and Hart<sup>11</sup> of creating a window between the anomaly and the adjacent bowel, may be necessary because of the poor condition of the patient or the location of the anomaly.

#### SUMMARY

I. Six cases of duplication of the alimentary tract are presented. Successful resection of the anomaly together with the contiguous intestine was accomplished in five and excision was performed in one.

2 The condition is more commonly seen in infancy and childhood than in the older age-group, and more commonly in males than in females

3 It is suggested that duplications of the alimentary tract are not as rare as previously supposed and should always be considered in the differential diagnosis of massive intestinal hemorrhage in the younger age-group. Four of our cases presented severe hemorrhage as the first symptom

4 With proper preoperative management, resection or excision of these anomalies can be performed with complete relief of symptoms

We are greatly indebted to Dr Dorothy H Andersen, Associate Pathologist at Babies Hospital, for her kind assistance with the pathologic reports and for the photographs

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# A PSYCHIATRIC STUDY OF SIXTY-ONE APPENDICECTOMY CASES\*

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SURGEONS, and the medical profession generally, have long realized that emotional disturbances of varying depth and intensity may accompany disorders requiring surgery. Marked anxieties, hysteria, and a whole catalog of neurotic manifestations are commonly encountered, both preoperatively and to a lesser extent, postoperatively. Until quite recently, however, the nature and origins of these emotional disturbances were not fully appreciated. They were either completely neglected, or regarded merely as natural by-products of a surgical experience admittedly harrowing to the patient.

In January, 1943, the Department of Surgery of Vanderbilt University Medical School, with a view to widening the borders of knowledge in this field, began a study of certain surgical problems where the emotions seemed to play a rôle. The purpose of this study was to discover, clinically, how the emotions enter into the etiology, treatment and convalescence of surgical patients and to determine how psychiatry can aid the surgeon in curing the patient. Implicit is the assumption that every sick person has a psychologic as well as a somatic aspect to his illness.

This paper is based on the study of 61 consecutive admissions of patients operated upon for appendicitis.

## DESCRIPTION OF PATIENTS

Our patients were white men and women, all between the ages of 16 and 55, from the Middle Tennessee hill section. They showed a wide variation in schooling and intelligence. The fact that most of these patients, and their parents before them, were more or less permanent in their residence made it easier to get complete family histories and to carry on follow-up studies.

The majority of the Middle Tennessee hill people are of Scotch-English descent, their native reserve and emotional control is somewhat comparable to that of the American Indian. Whatever attitudes of fear, anxiety and grief that the patients might hold, they usually appeared calm and unperturbed. Occasionally their reserve was so great as to be virtually impenetrable. Nevertheless, since the authors have lived in this section, our rapport with patients was usually sufficient to enable us to detect their emotional motivations, allay

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much of their preoperative worry and help in doing away with postoperative anxiety

#### PROCEDURE

We could only occasionally make preoperative psychologic studies, since most of the patients were operated upon as soon as possible after a diagnosis of appendicitis had been made. Usually, though, we could see the patient briefly before operation and observe him for signs of anxiety. For the most part, we were able to take some steps toward relieving this anxiety and make the patient's adjustment to the operation easier.

Then, about 12 hours after the operation, systematic psychologic studies were begun. We secured personal and family histories from the patients and their relatives. These histories brought out many details which bore directly or indirectly upon the understanding of patients' emotional adjustment.

The use of the Wechsler-Bellevue and Stanford-Binet intelligence tests, not only gave us the level of the patient's general intelligence but also told us much about his patterns of belief and his reactions to failure, success, praise, fatigue and illness. The reactions of the patients to test material gave evidence of the presence or absence of anxiety; if anxiety was present, we had to decide whether it was temporary or associated with some basic personality picture.

We also made consistent use of the Rorschach method to gain a knowledge of the patient's basic personality trends and deviations which were, in turn, leads for further clinical investigation.

After all psychologic studies were finished and the case history as complete as possible, we studied the data and then began psychiatric interviews with the patient. Often these interviews lasted over several weeks. We encouraged the patient to talk about his home, his relationships toward his family and friends, his work or school experiences—anything in his life which might have a bearing on his attitude toward the illness. We discussed the patient's dreams, moods and thoughts. We had the patient describe his anxieties before the operation, his attitude toward the anesthesia and anxieties after the operation. We carried on a sort of modified mental analysis, by which we were generally able to resolve many of the patient's worries and help him through his convalescence. Naturally, if anxiety is aroused, one factor in the patient's recovery is his ability to handle this anxiety.

We also obtained the surgeon's views on the patient's physical condition and emotional attitudes. The observations of the psychiatrist, the psychologist and the surgeon were all taken into consideration. This combination provided a basis for coming to grips with the problem of anxiety and its relation to the experience of an appendicitis operation.

#### MEANING OF THE OPERATION

The present-day attitude of the public toward surgery has an important bearing on the attitude of the individual patient. As recently as 20 years ago, people felt that when a person was taken to the hospital to be cut open he was

as good as dead. Today, the public, even in these backward hill sections, has confidence in the surgeon. Conscious anxiety over the outcome of an operation is materially lessened, and the individual patient facing a surgical operation has little fear that death will result.

Anxiety remains, however, in the *unconscious mind*. In his unconsciousness the patient sees the surgical operation as an attack upon his safety, which is to result in a grievous wound upon his body. To consent to such a thing the patient must reach a stage of complete acceptance. He will have to put himself entirely in the hands of the surgeon, and when general anesthesia is used, he will have to be willing to allow himself to be made unconscious. Even though his conscious mind may see the necessity of the course, the unconscious mind often cannot achieve the passivity necessary to accept such a death-like state without some fear and opposition.

To counterbalance this, however, other attitudes influence the degree of this fear and opposition. For instance, an operation is an exciting event in the life of a person whose emotional outlook is limited; it is a dramatic episode that gives temporary respite from the hard work and dullness of a life of poverty; it necessitates attention and care. Often such considerations are so strong that the patient welcomes the operation. Again, a certain type of neurotic patient may welcome an operation because, to the unconscious mind, it represents a physical punishment. Such patients have carried over from childhood a deep-seated sense of guilt for some real or fancied sin. So, to the unconscious mind, the operation is a means of atonement.

To atone for such a sin, a certain kind of neurotic patient has an unconscious wish to be emasculated. To such a patient removal of the appendix is a symbol of emasculation and results in a feeling of satisfaction. To some neurotic women the appendicectomy represents an abortion or a delivery. It, therefore, fulfills an unconscious wish.

Most people realize that the appendix is a useless organ which may, without notice, cause them illness. Therefore, when the pain and inconvenience are over, the average person is glad to be rid of such a potential threat of disease. All too frequently, however, the patient's attitude is markedly neurotic, characterized by intense fear, depression, anxiety and hysterical symptoms. During our psychiatric interviews with the 61 patients, we endeavored to find the basis for these attitudes. Then we went about reorienting the patients by giving them some insight into their problems.

#### RATINGS

For this study we classified the patients according to their degrees of anxiety, rating them as A, B, C, D and E (Table I). The anxiety of patients in the first three ratings is considered non-neurotic. The last two ratings are in the neurotic range.

In Rating A falls the patient with no particular anxiety. Such patients thought of little besides their severe pain, and the operation, even though it

might otherwise have held some dread, was welcomed as a release from the pain. Twenty-three per cent fell in this group.

In Rating B are those who showed a certain amount of anxiety before the operation, as evidenced by their anxious facies, vasomotor instability, overtalkativeness, *etc.* These patients reacted very well postoperatively and regained their physical and mental equilibrium with ease. Fifteen per cent fell in this group.

A third group of patients, in Rating C, has a considerable amount of *repressed* anxiety when relieved from the severe pain which they were suffering. Part of this was derived from a definite cultural pattern, since these Tennessee hill people habitually repress emotional expression. Thirteen per cent fell in this group.

TABLE I  
PATIENTS BY RATINGS

	Number of Patients	Per Cent of Patients
Non neurotic		
(A) No marked anxiety	14	23%
(B) Preoperative anxiety with postoperative relief	9	15%
(C) Repressed anxiety with welcome relief from pain	8	13%
Neurotic		
(D) Hysterical reaction (anxiety hysteria)	11	18%
(E) Marked anxiety aroused not relieved postoperatively (anxiety neurosis)	19	31%
Total	61	100%

Then, in the decidedly neurotic range is Rating D, composed of patients who reacted with an hysterical pattern. Such people often showed marked anxiety and fear. The convalescence of those in this rating depends considerably upon the attitudes of their families and those about them. They were usually emotionally dependent persons, whose hysterical attitudes had been nurtured by their families since early childhood. In this group, too, fall many of the well-known surgical cases where physical symptoms are produced directly by an emotional conflict. In other cases the hysterical reaction is not quite as clear-cut. Sometimes the operation obscures this hysterical reaction for the time being. Thus, it is only after recovery that we can detect the basic hysterical pattern. Eighteen per cent fell in this group.

Finally, in Rating E are a certain number of patients who reacted with marked anxiety. These patients had an anxiety neurosis of long-standing which was heightened by the experience of a surgical operation. Such a patient leaves the hospital with an additional psychologic handicap. The wound heals but the anxiety is increased and the pain often remains. Thirty-one per cent fell in this group.

DIAGNOSTIC GROUPS

To compare the actual illnesses of these variously reacting patients, their disorders are classified into two groups (Table II) Group I includes the cases of (1) acute appendicitis, and (2) other cases of abdominal disease sufficiently serious to cause an appendicitis-like pain in the right lower quadrant—such disorders as ileitis, ruptured graffian follicles, cystitis, pyelitis, *etc*

In Group II fall the cases of (1) chronic recurrent appendicitis, so classified when there had been some history of appendicitis attacks but where no acute inflammation of the appendix was found at the time of operation, and (2) undiagnosed disease of the abdomen, so named when neither the surgeon nor the pathologist reported any gross or microscopic lesion in the appendix and where no other pathologic condition of the abdominal organs was found *All of the patients in Group II, it might be noted, were in the D and E ratings—the neurotic range* (Table III)

TABLE II  
PATIENTS BY DIAGNOSTIC GROUPS

	Number of Patients	Per Cent of Patients
Group I		
(1) Acute appendicitis	36	59%
(2) Other abdominal disorders	8	13%
Subtotal	44	72%
Group II		
(1) Chronic recurrent appendicitis	4	7%
(2) Undiagnosed disease of the abdomen	13	21%
Subtotal	17	28%
Total	61	100%

CASE REPORTS

**Case 1**—An example of Rating A was No 47, a 17-year-old girl, of good intelligence Slight and undernourished, she had a very difficult life Child of separated parents, she worked in a factory eight hours a day and then came home to four or five hours of housework She had recently had an even more difficult time of it when her sister had been in the hospital with appendicitis While her mother cared for the sister, the girl had to pay the expenses of her sister's operation out of her own meager wages Psychologic tests revealed stereotyped, immature responses, but not those of a person with any hysterical mechanism Her condition was acute appendicitis, and she was suffering so much pain that she welcomed the operation without apparent anxiety She complained very little, said she was not frightened, and the postoperative course was uncomplicated

**COMMENT** Apparently to this patient the operation meant a relief from her hard, ugly, everyday life It meant good care and attention with a welcomed release from pain Her attitude toward surgery was entirely non-neurotic

**Case 2**—Rating B is well illustrated by No 58. This patient showed a great deal of anxiety before the operation, knowing something of the circumstances of her life we could have mistaken her illness for an hysterical mechanism to escape marriage. The facts were, however, that she and her fiancé had consummated their marriage the week before and were to have been married on the day of her operation. Feeling that she was already married in all but name the patient had the feeling of being torn from matrimony and this was the apparent cause of her worry. She was a spoiled only child, quite stubborn and negative. Her medical history showed several previous attacks of appendicitis, but she had refused to have the operation performed until the condition became acute and the appendix was ruptured. After the operation the patient made a rapid recovery.

**COMMENT** Though the effect of the operation had been to arouse anxiety, this patient had the resources to regain emotional equilibrium quickly. She was very proud of the successful way she came through the ordeal.

TABLE III  
PATIENTS BY RATINGS AND DIAGNOSTIC GROUPS

Ratings	Group I (Appendicitis)		Group II (Not appendicitis)	
	No	Pts	No	Pts
Non neurotic				
(A)	14	32%	0	0%
(B)	9	20%	0	0%
(C)	8	18%	0	0%
Subtotal	31	70%	0	0%
Neurotic				
(D)	0	0	11	65%
(E)	13	30%	6	35%
Subtotal	13	30%	17	100%
Total	44	100%	17	100%

**Case 3**—No 25 was a good example of Rating C, showing a good deal of repressed anxiety but remaining in the non-neurotic range. This was a boy, age 16, reared in a primitive community, suspicious of strangers and new situations. His appendix was found to be gangrenous and perforated and, after the operation, the patient had a difficult time for several days. Psychologic tests showed a great amount of anxiety and fear but this was inhibited. One incident illustrated the boy's reserve and suspicion. He lay on his arm for so long that his hand became temporarily paralyzed but he said nothing about it until the condition was accidentally discovered by the psychologist. The patient's dread of the operation was overcome by severe pain, so that he repressed, or blocked-off, his anxiety. During his convalescence he was less sullen, almost cheerful, and after a time said he felt all right and wanted to go home.

We come now to some examples of patients who reacted to surgery in a neurotic way and patients whose neurotic patterns actually gave rise to their physical symptoms.

**Case 4**—An interesting example of Rating D (those patients with an hysterical pattern) was No. 12. This was an intelligent Army student who was taking a course in meteorology at Vanderbilt University. Psychiatric interviews showed that he was abnormally attached to his mother and that, as a defense against this, he had turned his affections toward his father. His medical history showed a predilection toward upset stomach and mucous colitis. The vasomotor system showed some instability.

The patient's illness was real enough, with acute pain, tenderness, and nausea. While the surgeons were not sure that he had appendicitis, they considered the fact that he was in the Army and might have an attack at some future time less favorable for operation. Thus, they agreed to operate, and found that the appendix was entirely normal. The boy's attack appears to have been of hysterical origin, abetted by suggestion. Several of his Army friends had had their appendices removed and he had discussed the operation with them. They all agreed that it was a good thing to have the appendix out, because they might have an attack sometime while they were overseas and away from a hospital. (Latent homosexuality—a desire to "be like his buddies," may have been an element here.)

**COMMENT** The suggestibility of this patient was a factor in his short and satisfactory convalescence. He accepted psychotherapy readily. We talked over the case with him quite frankly so that he was much better fitted to meet his emotional situation than he was before he came in.

What attitude should the surgeon take toward patients who show symptoms of appendicitis and undergo operations but where there is no disease of the appendix? The Surgical Staff at Vanderbilt University Hospital believe, and we concur with them, that in such cases the facts should be revealed frankly to the patient if his intelligence and emotional make-up permit. The hysterical mechanism should be thoroughly explained to the patient so that he will be able to meet life on a less neurotic basis. If this is not done, the chances are that the pain will return and there will be symptoms which may expose the patient to more surgery.

The soldier patient described above was an intelligent young man, with whom we were able to work effectively. However, more than half of the patients, in whom we found no disease of the appendix, were mentally defective or borderline cases. With persons of such limited intelligence, complete frankness is not desirable since it would only create further anxiety. But even such patients can be helped by suitable psychotherapy.

**Case 5**—Also in Rating D was No. 32, a young woman whose illness represented an hysterical attack. She was a woman of dull-normal intelligence, whose hysteria arose from her compelling wish for a child, long frustrated because of her husband's impotence. She had separated from her husband and was living with another man. She pictured the operation in her mind as being the delivery of a child. Her appendix, on removal, was found to be entirely normal. It was a case of phantasy pregnancy, hysterically motivated.

**Case 6**—No. 10 illustrates Rating E, including patients with severe anxiety neurosis. This was a 27-year-old woman whose history of weight loss, nervousness, and slightly enlarged thyroid suggested hyperthyroidism. She had acute inflammation of the appendix with gangrene of the distal half. She also had pyelitis on the left side. The patient was very tense and suffered considerably after the operation. On the fourth day she was taken with a deep anxiety about her children at home, and insisted on leaving the hospital to go to them. The children were being adequately cared for by the patient's sister, and there was no need for her anxiety.



Psychiatric interview brought out the fact that she had once induced an abortion. She felt, she said, that she had committed a great sin. She had asked God a thousand times to forgive her. She had never wanted children and was reluctant about having marital relations because of her fear of pregnancy. Our psychiatric interviews showed that she had definite death wishes toward her children and as a result felt a deep guilt. Unconsciously, the operation represented some atonement for sin.

COMMENT: This patient is an example of the bodily punishment attitude some neurotic patients display toward surgery, and one in which we had most gratifying success. We explained to her the basis of her anxiety, and she had some conferences with a minister who is familiar with psychiatry. When she was seen again about three months later, she had gained weight, looked years younger, and seemed to be almost entirely free of her former anxiety.

CASE 7—No. 43, a 34-year-old male, from an isolated rural section, who had symptoms of appendicitis, was another case in Rating E, but whose appendix was found to be normal. He was a sexually maladjusted person with a long-standing anxiety neurosis. He complained that his wife "ran around", he had erotic pictures tattooed on his arms, and he suffered from a feeling of sexual inadequacy coupled with a marked sense of guilt for what he considered sexual transgressions in the past. Psychiatric interviews with this patient brought out the fact that he had an unconscious wish to be castrated in order to atone for his guilt and resolve his sexual maladjustment. He feared castration, also, but the wish was stronger than the fear. His neurosis took the form of an appendicitis attack, but to his unconscious mind the operation connoted emasculation. A month after he left the hospital he said he was "puny" about the legs and hips, and complained of being "no good."

Patients with neurotic patterns do not invariably react to surgery with anxiety, however. Patient No. 17 (Case 7) is an instance in point.

CASE 7—No. 17. This patient was an extremely neurotic man, who reacted to surgery without the least anxiety—in fact with great pleasure! He was an hypochondriac who had been coming to the hospital for 20 years with one complaint or another. Pain in the chest, smothering spells, palpitation of the heart, dyspnea and precordial pain, especially pain in the epigastrium, "spreading all over the abdomen" was the way his medical chart read. He was always having trouble with his "stomach." One afternoon he came in with especially severe pain in the lower right quadrant. The intern, knowing his neurotic history, gave him some sedative pills and told him to come back in the morning. In the morning, the examining surgeon ordered the man to the operating room, where it was found that the appendix had ruptured. He remarked, sagely, that appendicitis was a bad thing for a neurotic to have.

Coming out of the anesthetic our patient was a happy man. His attack of honest-to-God appendicitis proved that he had really been sick all those years. "I always knew there was something wrong with me," he exulted. "I always knew there was something there that needed to be cut out with a knife."

A postscript to this case is that after being sent home the patient had a recurrence of the characteristic pain he had before his appendectomy. He is not yet cured.

#### CONCLUSIONS

The surgeon should not be satisfied with only a mechanical operation upon the body which often fails to *get the patient well*. This is true whether the

patient has an acute surgical disease or whether he is showing hysterically originated symptoms simulating a surgical disease. A cure can be best assured when the surgeon-psychiatrist team carries out the following steps:

(1) Preoperative. It is important in every case that the surgeon talk with the patient before the operation, explaining what the operation consists of, the comparative lack of danger, and the procedure following surgery. Where there is a surgeon-psychiatrist team, the psychiatrist can also help in this work. This has a very desirable effect on the patient by reducing his preoperative worry, sometimes almost to zero.

(2) Postoperative. Psychologic studies continuing after the operation will indicate the amount and type of postoperative treatment required. In cases of hysteria where there is no clinical or pathologic abnormality found, it is essential to have some psychotherapy after the operation.

(3) Follow-up. In cases of deep-seated anxiety, it is evident that the patient should have follow-up treatment after he leaves the hospital, with visits by a social worker with psychiatric understanding, and possibly with continued visits to the psychiatrist. Without the follow-up treatment the patient's recovery will not be complete, nor his adjustment adequate.

This article covers only a narrow group of surgical cases—those patients suffering from appendicitis. If it shows that the surgeon needs a psychiatrist-psychologist-social worker-team in this emergency illness, how much more must this be true in chronic cases like tumors, ulcers, cancer, tuberculosis and bone diseases, where the patient's attitude is even more a factor in treatment.

Psychotherapy may not only prevent an unnecessarily prolonged convalescence after necessary operations but may reduce the number of patients having repeated unnecessary operations because of recurrence. For determining the importance of psychotherapy in surgery it seemed best to begin with a study of emotional attitudes of patients before, during and after surgery. This is not so clearly shown in the group of patients selected for this paper but will be demonstrated in other groups of less acute surgical cases studied by the authors, and which will be discussed in subsequent reports.

It was found that these psychiatric studies could be carried on in the wards of the Vanderbilt University Hospital with the full coöperation of the attending staff, residents, interns, nurses and, also, significantly enough, of the patients. We might point out that there was not a single case of objection to the program by a patient, and, in fact, many who were not included in the study felt that they had been neglected. There was not, as some had feared, friction among the staff members in relation to this study.

Most gratifying to all was the fact that the study interfered in no way with the vital relationship between patient and surgeon. This relationship, in conclusion, is as important as anything else in surgical treatment. The psychiatrist calls it emotional transference. In quite simple terms it means the patient's confidence, faith and trust in the doctor. Without this transference—this rapport—the patient's anxiety is likely to be a serious obstacle to smooth recovery. The patient is likely to have more pain before operation, to have

more difficulty with anesthesia, to be less relaxed during the operation, to have more pain afterwards, and to have a longer convalescence. Of course, the older, experienced surgeon knows instinctively the importance of this transference, and acts accordingly. But what we are attempting to do is to help the younger surgeon gain this technic without having to pick it up by years of experience. The presence of the psychiatrist at the surgeon's right hand, far from interfering with this transference, helps to make it more effective.

Of course, where a psychiatrist is not available, it rests with the surgeon to do the whole job of establishing rapport with the patient and dispelling his fears. But in large, busy wards, the psychiatric team is an essential part of the surgeon's staff, if the surgeon's aim is to heal the patient rather than simply to see him recover from an operative wound.

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# LOCAL PENICILLIN THERAPY IN SURGICAL INFECTIONS\*

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IN A SERIES of 142 patients with surgical infections treated with penicillin, 17 received local penicillin therapy alone 53 received a combination of local with systemic penicillin therapy, and 72 received only systemic penicillin therapy

Local penicillin therapy proved equally effective in the treatment of localized areas of infection and in the treatment of accessible localized foci associated with systemic manifestations of infection, particularly when the latter were in poorly vascularized areas or contained much nonviable, necrotic material Often the well-localized readily accessible infection could be treated with local penicillin therapy alone When accessible septic foci and systemic manifestations of infection were combined, local and systemic therapy were effectively given concomitantly Also in the prophylaxis of infection in operations in contaminated or infected fields a combination of local with systemic penicillin therapy proved useful Patients with systemic manifestations of infection or other signs of incomplete localization of infection always received systemic treatment with penicillin

Wherever it was possible to use local penicillin therapy alone or in combination with systemic penicillin therapy, this treatment appeared to be more effective and more economical than the use of systemic penicillin therapy alone Often penicillin-sensitive infections were controlled readily with relatively small doses of penicillin in concentrations of only 100 to 200 units per cubic centimeter of physiologic saline Relatively more resistant strains of organisms, which could not have been reached with the concentrations of penicillin obtainable in the blood stream by systemic therapy, often could be controlled by increasing the concentration of solutions given locally to several thousand units per cubic centimeter For most local therapy, concentrations of 100 to 500 units of penicillin per cubic centimeter of physiologic saline were used, but often concentrations of 5,000 to 10,000 units and occasionally concentrations of 25,000 units per cubic centimeter were used The use of high concentrations of penicillin in soft tissue defects apparently caused no harmful effects, but was avoided unless necessary Concentrations in excess of 1,000 units of penicillin per cubic centimeter of physiologic saline were never used in areas that communicated with the central nervous system or the linings of

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serous cavities, unless the infected area was walled-off from the normal tissue by a well-established wall of granulations or pyogenic membrane

It was necessary to observe very strict aseptic precautions during dressings and injections to avoid the introduction of penicillin-resistant organisms into the area under treatment. The normal processes of autolysis appeared to resolve nonviable débris quickly, once the infection was controlled with local penicillin therapy in small, well localized infected areas, but resolution occurred more rapidly if the débris was removed by some mechanical method, such as aspiration or surgical operation. In larger areas, and particularly in very irregular areas containing numerous ramifications, the use of surgical methods to eliminate nonviable tissue and other débris resulting from infection was found to be necessary.

TABLE 1

RECORD OF A PATIENT WITH AN ABSCESS OF THE SCALP FROM HEMATOGENOUS OSTEOMYELITIS OF THE OCCIPITAL SKULL TREATED WITH ASPIRATIONS OF PUS AND LOCAL INSTILLATIONS OF PENICILLIN SOLUTION (5 000 UNITS PER CC) FOR INVESTIGATIONAL PURPOSES. SYSTEMIC PENICILLIN THERAPY WAS WITHHELD UNTIL THE ABSCESS WAS CONTROLLED WITH LOCAL THERAPY.

Date	Material Aspirated	Penicillin Dosage	Bacteriologic Culture
9-21-44	12 cc thick yellow pus	25 000 units	<i>Hemolytic Staph aureus</i>
9-22-44	5 cc hemorrhagic yellow pus	25 000 units	<i>Hemolytic Staph aureus</i>
9-23-44	7 cc thin hemorrhagic pus	25 000 units	Sterile
9-24-44	5 cc thin hemorrhagic pus	25 000 units	Sterile
9-25-44	2 cc thin turbid slightly hemorrhagic pus	25 000 units	Sterile
9-26-44	1.5 cc thin turbid brownish fluid	10 000 units	Sterile
9-27-44	1.5 cc thin turbid yellow fluid	10 000 units	Sterile
9-28-44	Few drops of thin blood stained fluid	2 000 units	Sterile
9-29-44	1 cc thin yellow fluid	10 000 units	Sterile

Usually local instillations of penicillin solution once or twice daily sufficed to control, in a few days, infections in walled-off abscesses or in wounds that had been closed. In wounds that were open or partly open, penicillin solutions did not remain in contact with the infected areas long enough to be effective, and it was more desirable to dress the area once or twice daily with an ointment or jelly containing penicillin (usually 500 to 1,000 units of penicillin per Gm), rather than to attempt frequent dressings or instillations of penicillin solutions. In the presence of penicillin-resistant organisms it was preferable to remove the purulent secretions from the wound and instill penicillin solutions at more frequent intervals, usually three to six hours apart. On two occasions local therapy was given by continuous slow drip infusion (100 units per cubic centimeter of physiologic saline solution), and this method was effective, but cumbersome. In some wounds heavily contaminated with organisms that were markedly resistant to penicillin, other agents had to be used to control the infection.

Effective local penicillin therapy required the services of skilled personnel, and the procedures associated with local treatment with penicillin often consumed much of the time of the attending surgeon. In small, well-localized areas of infection, such as small abscesses, the procedure of aspiration and

local instillation of penicillin solution was applicable (Tables I and II). The skin was prepared by cleansing with a detergent solution. A sterile tray containing two syringes and several sizes of needles was prepared and aseptic precautions were observed throughout the procedure. The penicillin solution was drawn into one syringe, which was temporarily placed aside. With the second syringe and a fine needle, a small procaine wheal was made in the skin at the proposed site of aspiration and the deeper tissues were anesthetized if necessary, then a larger needle (usually No. 18 or 16) was applied to the syringe and introduced into the infected area, and as much of the purulent material as possible was aspirated. The contents of this syringe were used for bacteriologic cultures. The syringe containing the penicillin solution was then fitted to the needle and the abscess cavity partly filled with penicillin solution. The amount of penicillin solution introduced into the abscess cavity usually

TABLE II

RECORD OF A PATIENT WITH A CERVICAL ABSCESS ARISING FROM OSTEOMYELITIS OF THE MANDIBLE TREATED BY ASPIRATION OF PUS AND LOCAL INSTILLATIONS OF PENICILLIN SOLUTION (5,000 UNITS PER CC.) NO SYSTEMIC THERAPY

Date	Temperature	Material Aspirated	Penicillin Dosage	Bacteriologic Culture
5-2-45	102° F	38 cc. thick foul grayish pus	50,000 units	<i>Anaerobic Staph</i> and <i>Strep</i> , <i>Actinomyces</i> , <i>Bacteroides</i> and fusiform <i>Bacilli</i>
5-3-45	Normal	45 cc. more fluid hemorrhagic purulent material	25,000 units	<i>Anaerobic Staph</i> and <i>Strep</i> , Gram-negative filaments
5-4-45	Normal	45 cc. thin hemorrhagic fluid	50,000 units	<i>Anaerobic Staph</i> and <i>Strep</i> , Gram-negative filaments
5-5-45	Normal	20 cc. thin serous fluid	50,000 units	<i>Anaerobic Staph</i> and <i>Strep</i> , Gram-negative filaments
5-6-45	Normal	20 cc. thin serous fluid	25,000 units	No growth
5-7-45	Normal	5 cc. thin yellow serous fluid	25,000 units	No growth

was several cubic centimeters less than the amount of pus removed, in order to avoid leakage from the puncture wound after withdrawal of the needle. The site of puncture was sealed with a drop of collodion. Aspirations and injections usually were repeated at 24-hour intervals during the first three or four days of treatment, and after that they were repeated as often as fluid could be obtained.

In infections with penicillin-sensitive organisms the cultures usually became sterile after about 48 hours of local treatment with penicillin. However, it was found to be desirable to continue aspirations and penicillin instillations as long as fluid could be obtained, in order to avoid recurrence of the infection. After two or three treatments the contents of the abscess cavity usually became thin, serous and slightly hemorrhagic in character, and a smaller needle (No. 20 or 22) could be used for the treatments. This closed method of treating small localized infections was valuable because it permitted the penicillin solution to remain in contact with the infected area for long periods, prevented contamination with penicillin-resistant organisms, and often obviated the necessity for surgical incision.

This method was not suitable for large infected areas, those with ramifications, or those containing considerable amounts of débris that could not be aspirated. In such cases it often was possible to carry out a surgical procedure in which the area was drained through an appropriate incision, all unattached debris carefully removed by irrigation with physiologic salt solution, one or more soft rubber tubes placed in the main cavity and one into each ramification or recess, and the wound closed with a few sutures placed through all layers. The rubber tubes were brought out through a small aperture in the sutured wound or through a small separate incision, and were carefully covered with sterile dressings. Penicillin solution was introduced into the wound through them once or twice daily, the strictest aseptic precautions being used to prevent contamination (with penicillin-resistant organisms). The amount of penicillin solution to be introduced at each instillation was determined at the time of completion of the operation, as it was unnecessary and undesirable to introduce excessive amounts that would serve no useful purpose, and would merely run out of the wound and saturate the dressings. The incisions in these cases were intentionally placed with the object of retaining penicillin solution within the wound (in sharp contrast with the orthodox objective of placing incisions to obtain free dependent drainage). The penicillin tubes usually were removed on about the 7th to 10th postoperative day, and always were withdrawn by the 14th postoperative day. This method proved to be very useful in controlling large and irregular localized areas of infection, prevented secondary contamination with penicillin-resistant organisms, and permitted early healing and restoration of function. However, it must be stated that the outcome of cases treated in this manner depended considerably on the skill and care of the attending surgeon, with particular reference to the thorough completion of the operation and meticulous asepsis in handling the penicillin tubes and dressings postoperatively. All of the patients receiving this type of local penicillin therapy were protected against the possibility of dissemination of infection by preoperative and postoperative systemic penicillin therapy.

Following operations in contaminated areas the wounds often were closed around the ends of soft rubber tubes that had been placed in the depths of the wounds, and penicillin solutions were injected into the wounds through the tubes once daily for seven to 14 days (and rarely longer) postoperatively. Continuous penicillin drip also was used in connection with this method in a few cases. In the group treated by this method some of the wounds containing mixed infections suppurred, but the bacterial flora from such suppuration usually caused only some temporary delay in the healing of the soft parts. This type of treatment was not done at once in wounds containing *Proteus* organisms, instead, the wounds were left open and treated by some other method, and secondary closure was done after *Proteus* organisms had been eliminated. It proved to be much easier to prevent contamination of wounds, by careful aseptic technic during dressings and in handling the tubes during penicillin instillations, than to eliminate the troublesome (but usually not dangerous) penicillin-resistant organisms once they became established. All operations of

this type were preceded and followed by courses of systemic penicillin therapy, in order to avoid the possibility of dissemination of infection

In cases in which it was necessary or desirable to treat open wounds locally with penicillin, ointments or jellies containing 500 to 1,000 or more units of penicillin per Gm were used. It was necessary to assay the potency of commercial and laboratory-made penicillin preparations of this type, in order to be certain of their efficacy. In several instances, when effective penicillin preparations were not available, the pharmacist prepared a suitable sterile ointment or jelly base and the surgeon mixed the penicillin solution into the base immediately before applying it to the wound. Open wounds that suppurated considerably required careful cleaning and dressing several times daily. As the wounds became cleaner, the dressings and application of penicillin ointments could be done once daily. This method of treatment was impractical for large open wounds, and it proved to be somewhat laborious, though quite satisfactory and economical, for patients with small open infected wounds in which the predominating pathogen was sensitive to penicillin within the range of potency obtainable in the wound.

Infected serous cavities, such as joints, usually were aspirated and instilled with penicillin solution once daily. For local instillation in serous cavities the concentration of penicillin was usually limited to 1,000 units per cubic centimeter of saline, but higher concentrations could be used in areas where isolated, walled-off abscesses were present. The strictest aseptic technic was maintained in the treatment of infected serous cavities.

In wounds involving the meninges and central nervous system, concentrations of 500 to 1,000 units of penicillin per cubic centimeter of physiologic saline were usually used. All injections of penicillin solution into the subarachnoid spaces were made by lumbar puncture, after first draining all the cerebrospinal fluid that would flow freely. The dose used for intraspinal injection varied from 5,000 to 20,000 units given once or twice daily. Daily bacteriologic cultures were made. The small dose of 5,000 units appeared to be as effective as larger doses of 10,000 to 20,000 units in most infections of the central nervous system. Systemic penicillin therapy also was given in all such cases.

#### SUMMARY

Small, well-localized pyogenic abscesses may be treated successfully with aspiration and instillation of penicillin solution. Larger areas of localized infection, especially those with ramifications and those containing much thick, purulent material or necrotic debris, require incision for evacuation. In some of these the incision may be closed at once around tubes through which local penicillin therapy is given, others may require delayed closure. Infections in well-localized areas may be treated with increasing concentrations of penicillin solutions until resistance of the infecting organism is overcome.



# A SUCCESSFUL METHOD FOR SECURING PRIMARY WOUND HEALING AFTER RESECTION OF FISTULAE IN ANO

A PRELIMINARY REPORT

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THE COMMON AND ACCEPTED METHODS for treating a fistula in ano have always appeared to the author to be archaic and not at all in keeping with modern surgical technic. In fact, they have not appreciably advanced beyond the principles laid down a hundred years or more ago. In the usual procedures described in the literature and in popular textbooks on Surgery and Proctology, the tract is opened widely, destroyed, and the resultant wound then allowed to granulate, that is, heal by second intention. When the tract passes through or under the external sphincter, that muscle is severed by one of several methods, and then nature trusted to unite the cut-ends, something which, to the chagrin of the surgeon, does not always take place. The convalescent period after this type of operation is commonly marked by its length, discomfort, temporary anal incontinence, frequent dressings and sitz baths and the need for careful and prolonged wound care to insure proper healing. If the cut-ends of the sphincter fail to unite properly, either a second operation must be performed, or the patient will suffer from some degree of anal incontinence—a constant source of potential embarrassment. When fistulae are extensive, the scar tissue laid down after this type of operation may be such that the patient is seriously handicapped either in sphincteric control or else by virtue of stenosis. Therefore, it seemed very desirable to develop a surgical technic in which it would be possible to excise the tract and close the wound so that healing by primary intention would take place, and, thus, avoid the many undesirable features associated with the methods now employed. This has been done. Twelve patients have had a fistula in ano resected and the operative wound closed tightly, with healing by primary intention in 11 cases. In the twelfth case, the procedure to be described was not followed in all of its component parts. The convalescent period in the 11 cases was marked by its freedom from pain or discomfort, its shortness, the absence of drainage, and the lack of need for time-consuming care and treatment. There have been no recurrences during follow-up periods of from two to six months.

## MATERIAL

The patients were all young adults between the ages of 18 and 31. Each had a history of an acute ischiorectal abscess which had had to be incised and drained. This had been followed by either one or more recurrences of the abscess or else by fairly persistent drainage from the site of the original incision. When first examined, each patient presented a true fistula in ano, with an

external orifice from which pus could be expressed and through which a probe could be passed and manipulated into the anal canal. Several patients had one or more branches to the primary tract.

#### METHOD

The patients are prepared for the operation in the usual manner, by sitz baths, low-residue diet, sulfasuxadime, and castor oil the afternoon preceding surgery. The evening preceding surgery the tract is injected with methylene blue in an effort to stain it so that all branches of the main fistulous tract can be readily identified during the operation. If it is believed that multiple tracts are present, the external orifice is injected with lipiodol and roentgenograms taken. All operations are performed in the flexed prone position, under either spinal or caudal anesthesia. After suitable preparation and draping of the operative field, a malleable, blunt-tip probe is passed along the tract and gently manipulated until it enters the anal canal through the internal orifice of the tract. The probe is then bent so that it forms a circle, and, thus, cannot be dislodged during the operation. A small elliptical incision is made around the external orifice down to subcutaneous tissue and one limb carried toward, but never across, the mucocutaneous juncture. A second small elliptical incision is made through the mucosa around the internal orifice, but skin and mucosal incisions are not joined. With a small, sharp, curved, dissecting scissors and a small knife (No. 15 Bard-Parker), the tract is gently dissected free from the surrounding structures, using the probe as a guide. Gentle traction assists in this. The tract is followed over, through, or under the external anal sphincter, doing as little damage as possible to this muscle. When the muscle is cleared from the tract, the internal orifice is attacked and dissection begun there and carried down until the tract is entirely freed, and can be removed *in toto*. The wound is carefully inspected for residual scar tissue, or for an undiagnosed limb of the fistula, either of which must be excised if present. Complete hemostasis is secured using Nos. 80 or 120 cotton ties. The tissues of the wound are then infiltrated with a penicillin solution, 2000 units per cc., using 20 to 100 cc. to insure equal and thorough diffusion throughout all the tissues. The dead space is very carefully obliterated with interrupted sutures of Nos. 60 or 80 cotton, repairing at this time any damage done to the sphincter. As it is of utmost importance that every vestige of dead space be obliterated, these should be fairly close together, as a rule, two or three layers will be necessary. The cut-edges of mucosa are carefully approximated with several Nos. 4-0 chromic catgut sutures on an atraumatic needle, and the skin edges are approximated with No. 60 cotton, using vertical mattress sutures in each instance. No drains are used. The postoperative regimen consists of a low-residue diet for 3-4 days, mineral oil daily, morphine, ice bag to the perineum for pain, and if no bowel movement occurs by the fourth day, an oil retention enema is given, followed by milk of magnesia orally. The patients are allowed to get out of bed on the second postoperative day, and discharged from the hospital shortly afterwards. The skin sutures are removed between the 5th and 7th postoperative days.

The essential points of the procedure, thus, are (1) accurate localization of the tract, (2) careful, neat dissection, (3) infiltration of the wound with penicillin, (4) complete hemostasis, (5) careful obliteration of the dead space with fine cotton sutures, and (6) complete closure of the mucosal incision. It is believed that if the technic outlined above is exactly followed, the results obtained can be readily duplicated.

### RESULTS

Of the 12 patients operated upon by this method, 11 have healed by primary intention. There has been very little edema of the wound, only mild postoperative pain, and there has been no drainage. There were no instances of even temporary anal incontinence. Nine patients were followed six months, or longer, and three patients were followed for two months. None have showed any evidence of recurrence of the fistula in ano. The one patient who did not heal *per primam* was not injected with penicillin at the time of operation. He complained of more discomfort than the average patient, and about the 5th postoperative day, the wound was red and swollen. Removal of the skin sutures permitted pus to escape. Drainage persisted until one or two cotton sutures were removed from somewhere in the depths of the wound, following which the wound healed. Letter follow-up indicates he has no apparent evidence of a fistula, but this case is classified as unsatisfactory. It illustrates perfectly the point that the outlined technic must be followed exactly if complications are to be avoided.

**DISCUSSION**—It is accepted by all surgeons that primary union is the ideal to strive for in any wound, traumatic or operative. This, because, when healing is by second intention, one must frequently contend with such undesirable features as infection, excessive scar formation, with consequent tissue distortion and malfunction, painful dressings, prolonged convalescence, and after fistulectomy, possible temporary or permanent anal incontinence. Furthermore, the scarring, distortion, malfunction, or in cases of fistulectomy, the anal incontinence, may require correction by secondary plastic procedures. It is recognized, of course, that certain wounds, for reasons inherent in themselves such as the repeated and heavy contamination that occurs around the rectum do not readily lend themselves to primary closure. Nevertheless, one should continually try to find new methods, or to apply recent advances, to the treatment of such wounds, in order that more of them, without increasing the risk to the patient, may be closed with a reasonable expectation of securing primary union. The method described in this paper does make possible the obtaining of primary union after resection of a fistula in ano. In addition to the common surgical principles of neat, clean, nontraumatic dissection and careful obliteration of all dead space, penicillin is carefully infiltrated into all of the tissues comprising the wound. The underlying principle of this procedure is to inactivate the bacteria in these areas, which, while not sensitive to the ordinary tissue concentration of penicillin secured by parenteral injection, presumably are inactivated by the extremely high concentration obtained in this manner.<sup>1</sup>

Cotton is used in preference to catgut because of the minimal tissue reaction to this material and, hence, less necrotic material to serve as culture media for the various organisms

Admittedly, the group treated is not large enough to permit any final evaluation of the method. However, it is a fact that 11 of 12 cases did heal by primary intention, and that the one failure was in the patient whose tissues were not injected with penicillin. This, in itself, indicates that the method should be practical if followed exactly. Furthermore, there have been no recurrences over follow-up periods of two to six months, probably a sufficient period of time for such cases. This would seem to indicate that the method is curative. There is no logical reason why there should not be just as many cures when fistulae are treated in this way, as by the method of laying them open to granulate in, provided all of the tract is excised.

There is also a great saving to the patient economically, because of early release from the hospital, lack of need to return for daily dressings, and the fact that he can return to his normal activities without experiencing the discomfort present when there is a raw, granulating, anal wound.

#### SUMMARY AND CONCLUSIONS

A successful method has been described by which it is possible to secure primary wound healing after the resection of a fistula in ano. The essential points in the procedure are (1) accurate localization of the tract, (2) careful, neat dissections, (3) infiltration of the wound with penicillin, (4) complete hemostasis, (5) careful obliteration of the dead space with fine cotton sutures, and (6) complete closure of the mucosal defect. Eleven of 12 cases so treated have had primary union of their wounds, and there have been no recurrences of the fistula in the 12 patients over periods of two to six months. The convalescent period was marked by its shortness, and absence of complications. The method described is preferable to those commonly employed in which healing is by second intention because it eliminates (1) excessive scarring, (2) anal incontinence, and (3) prolonged convalescence.

#### REFERENCE

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## THE EFFECT OF HEPARIN UPON INTRA-ABDOMINAL ADHESIONS IN RABBITS

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IT IS GENERALLY RECOGNIZED that certain patients form intra-abdominal adhesions after operation or after inflammatory processes. These may produce intestinal obstruction, and at times require surgery. Often adhesions reform and, again, cause obstruction. Methods that might prevent formation or reformation of adhesions have been the subject of several investigations adequately reviewed by Boys<sup>1</sup> in 1942.

Certain of these methods have been of general interest. Rea and Wangenstein,<sup>2</sup> Gepfert,<sup>3</sup> Totten,<sup>4</sup> Merkle,<sup>5</sup> and others, introduced amniotic fluid, saline, air, oil, glucose, blood, gum acacia, *etc*, into the peritoneal cavity to mechanically separate damaged surfaces until reepithelization might occur. Ochsner and Garside,<sup>6</sup> Donaldson,<sup>7</sup> Ward,<sup>8</sup> and others, tried proteolytic enzymes, such as papain or trypsin to digest deposits of fibrin. Lehman and Boys<sup>9, 10</sup> employed heparin to minimize the formation of fibrin. Clinical reports of the use of papain by Ochsner,<sup>11</sup> and of heparin by Lehman and Boys<sup>12, 13</sup> and Massie,<sup>14</sup> have offered encouragement, but the results are not easily evaluated.

Experiments have, therefore, been undertaken to further study the effect of heparin upon the formation and reformation of adhesions. Rabbits, usually male, have been used for all experiments.

### EXPERIMENTAL METHODS

*Operations for Production of Adhesions* Rabbits were anesthetized by intravenous sodium amytal. A midline incision was made, using sterile technic. The appendix was exposed and freed from the meso-appendix using fine silk No 000000, for ligation of vessels. The antimesenteric surface was then seared by applying a thin, heated spatula. The peritoneum and the incision were closed by a continuous mattress suture of either fine silk or catgut. The skin was closed with interrupted silk. Operations were performed by several individuals employing this standard technic.

*Operations for Division of Adhesions* Celiotomies were performed through the same midline incision two weeks, or more, after the sealing and at varying intervals thereafter, to determine occurrence and extent of adhesions and to divide and study reformation of adhesions. Adhesions were divided, using blunt dissection for closely adherent surfaces or sharp dissection with division and ligation for longer bands.

The extent of adhesions was determined by estimating the length of bowel involved and at times also by comparison of serial photographs. The length of extensively-involved matted segments of bowel was empirically estimated as 20 cm. The abdomen and chest were examined by autopsy in all animals that died. Histologic examination was made on the appendices of all animals sacrificed or dying within ten days of the original searing, and on other viscera that exhibited gross pathologic change.

*Technic of Control Experiments* Adhesions were examined at operation in two control series, but not divided. These adhesions were later observed at operation or autopsy. In a second control series the adhesions were divided without using any form of therapy and later reexamined.

*Method of Study of Heparin and the Formation of Adhesions* The effect of heparin on formation of adhesions was studied by searing the appendix and immediately placing 15 mg of heparin into the abdomen. A second intraperitoneal injection of 15 mg of heparin was given 24 hours after operation. In each instance the heparin was diluted by 30 cc of normal saline. Heparin in Pitkin's menstruum\* (100 to 200 mg) was placed in the abdomen at the time of searing in another group of rabbits.

*Method of Study of Reformation of Adhesions—Control Experiments* Reformation of adhesions was investigated in control experiments by administering 30 cc of normal saline intraperitoneally at the time of division and then twice a day by needle puncture for 72 hours. Gelatin, 5 per cent in sterile H<sub>2</sub>O, was similarly injected in another control series. The state of the adhesions was determined by subsequent operation or autopsy 7 days to 4 weeks, average 2 weeks, after division.

#### *Methods of Study of Reformation of Adhesions—Test Experiments*

(A) *Heparin in Saline* Heparin was administered in a volume of 20 to 30 cc of saline at the time of division of adhesions and subsequently at intervals during 72 hours by reinjection through the abdominal wall. Peripheral clotting time was determined on venous blood at intervals of two to four hours by the capillary-tube method. The initial 20 to 30 cc of saline contained 5 to 60 mg of heparin, usually 15 mg. Subsequent injections contained similar amounts of heparin. The usual total dose was around 200 mg. Intervals between injections were varied to maintain a prolongation of the clotting time always over two minutes and usually over 15. Maximum prolongation of clotting time was often one-half to two hours. Reformation of adhesions was studied during operation or autopsy in animals surviving seven to 60 days.

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\* The ingredients of the Pitkin menstruum are gelatin 15 to 30 per cent, dextrose 5 to 12 per cent, glacial acetic acid 0.5 per cent and sufficient distilled water to make 100 per cent. The formulae used in our paper were LP-8, LP-9, and LP-10. A reference for this information is Loewe, *et al*. Venous Thrombo-embolic Disease, J. A. M. A., Vol. 130, 388, February 16, 1946.

Heparin and saline (10 to 50 mg) was also administered at the time of searing and again by intra-abdominal injection at 24 hours in a group of rabbits

(B) *Heparin in Pitkin's Menstruum* Twenty-five to 200 mg was placed in the abdomen at the time of operation and subsequently injected during 72 hours at intervals determined by the peripheral clotting time. The usual total dose was around 300 mg. Prolongation of clotting time was maintained at levels similar to those described with heparin and saline. Heparin in Pitkin's menstruum (150 mg) was used as a single dose at the time of searing and also at the time of division of adhesions in other rabbits

#### EXPERIMENTAL RESULTS FORMATION OF ADHESIONS

*Production of Adhesions* One hundred and fifteen rabbits survived operation and searing of the antimesenteric surface of the appendix without infection. Of these, adhesions developed in 89. Twenty-six rabbits did not develop adhesions. Eighteen of the 26 were again treated by searing. Five developed minimal adhesions. Three developed adhesions only after the third searing.

*Formation of Adhesions* Adhesions developed in 15 of 21 rabbits in which heparin had been placed in the abdomen at the time of searing of the appendix and again injected 24 hours later. The appendices of five of the six animals that did not develop adhesions were again seared and when reexamined there were no adhesions. Adhesions developed in three of five rabbits in which heparin in Pitkin's menstruum had been placed in the abdomen at the time of searing. In five additional instances single doses of heparin in Pitkin's menstruum were administered at the time of searing. Adhesions formed in three.

*Duration of Adhesions* Seven rabbits were explored two weeks after searing, without dividing adhesions. Celiotomy 33 to 51 days later revealed no evidence of change in the amount or character of adhesions.

#### *Control Experiments—Reformation of Adhesions*

Reformation of adhesions was studied in the 89 rabbits that developed adhesions after the first searing. Since these rabbits were subjected to a series of operations during which adhesions were examined or divided and treated, or not treated, by control or test substances, and since they often served for from two to seven consecutive experiments the results will be reported as groups of experiments and not as individual animals. Animals dying within a week of operation, or developing infection, are not included in the experimental results.

(A) *Division of Adhesions without Treatment* Adhesions were divided in 18 experiments and subsequently reexamined. They reformed in all but one rabbit. The length of large and small intestine involved in adhesions before division varied from the attachment of a single band up to 20 cm,

average 6.9 After division the length varied from one band to 20 cm, average 9.0 cm. The extent of the adhesions observed after redivision had increased over that before division in ten experiments and decreased in eight.

(B) *Normal Saline* Adhesions were divided and treated initially by 30 cc of saline and subsequently by intraperitoneal injections of saline during 72 hours in five experiments. In four, adhesions reformed. The extent of adhesion before division varied from 2 to 20 cm, average 8. After division and treatment by saline the length of involvement varied from 0 to 10 cm, average 5. The extent of adhesions after treatment increased in two experiments and decreased in three. The rabbit that did not have adhesions after saline treatment had 20 cm before division.

(C) *Gelatin* Gelatin was used after division of adhesions in six instances and in five adhesions redeveloped. Before division of adhesions the length of involvement was from 2 to 18 cm, average 7. After treatment the length varied from 0 to 10 cm, and averaged 6. The extent of involvement increased in three and decreased in three. The animal that did not redevelop adhesions had one 3 cm band at the time of division.

#### *Experiments with Heparin—Reformation of Adhesions*

(A) *Heparin in Saline* In 20 experiments adhesions were divided and treated during 72 hours by heparin in saline. Adhesions reformed in 17. Before division and treatment adhesions involved 1 to 20 cm of bowel, average 8. Afterward they involved 0 to 20 cm, average 6. The amount of involvement increased in ten, decreased in eight, and was unchanged in two. The three animals that had no adhesions had had 1, 4, and 10 cm, respectively, at the time of division.

In addition to the 20 successful experiments there were eight deaths. Three were caused by hemorrhage.

(B) *Heparin in Pitkin's Menstruum* In 21 instances heparin in Pitkin's menstruum was employed during the first 72 hours after division of adhesions. They redeveloped in 19. The area of involvement before division and treatment varied from 2 to 20 cm, average 8.3 and afterward from 0 to 20, average 6.6 cm. The extent of adhesions increased in six, decreased in 11, and was unchanged in four. The two animals that did not redevelop adhesions had 4 and 10 cm, respectively, at the time of division of adhesions.

In four instances with single doses of heparin in Pitkin's menstruum given at the time of division of adhesions, all reformed them. The area of involvement varied from 6 to 15 cm, average 9, before treatment and afterward 2 to 20 cm, average 13. The extent increased in three and decreased in one.

In addition to the 25 successful experiments reported above there were 22 deaths during administration of heparin in Pitkin's menstruum. Of these 17 died of hemorrhage.

*Pathologic Examination*—Autopsies were performed on 15 rabbits sacrificed at intervals within ten days of searing of the appendix. Autopsies were also performed on 30 animals dying during or just after a 72-hour period of



treatment with heparin. Treatment was begun immediately after division of adhesions.

Gross examination of the 15 sacrificed rabbits often revealed fibrinous adhesions about the appendix. Material for staining and preparation for microscopic study was obtained from cross-sections of the appendix. Microscopic preparations satisfactory for study of mesothelium were obtained in

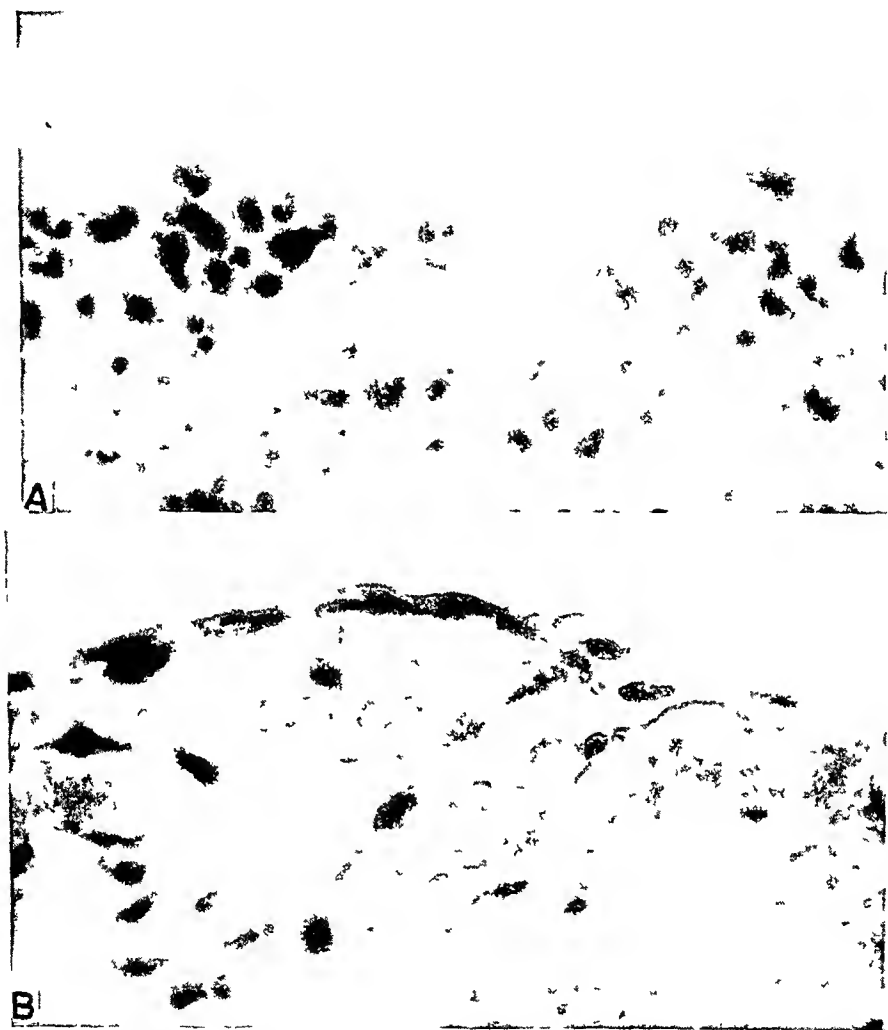


FIG 1—(A) Fibrinous surface of appendix 18 hours after searing  
(B) Fibrin covered by a single layer of flat cells resembling mesothelium 96 hours after searing

only seven. Of these two, six and 22 hours after searing, had no visible mesothelium. The burned surface was covered by fibrin (Fig 1 A). Two, at 18 and 42 hours, had a few isolated cells resembling mesothelial cells on the surface of the fibrin over the burned area. Three, at 30, 72, and 96 hours had continuous sheets of single-layered cells, resembling mesothelial cells, over the granulating surface (Fig 1 B).

Gross examination of 30 rabbits that died during the period of heparin therapy revealed massive hemorrhage into the abdomen or into the wound in 20. Satisfactory microscopic examinations of the appendices at the area of division of adhesions were possible in five of nine rabbits studied. Fibrinous exudate or fibrin was present in each. Sections of lungs of 12 showed advanced pulmonary edema. Congestion was also present in five, and hemorrhage in three. Brain tissue was examined in three and there were small hemorrhages in the pia mater of the cortex of two. One of two hearts examined showed small subendocardial hemorrhages in the left ventricle.

TABLE I  
SUMMARY OF STUDIES ON ADHESIONS

	No. of Experiments	No. that Developed Adhesions	% that Developed Adhesions	Change of Extent of Adhesions (Average)		Number of Animals Exhibiting Change		
				Before	After	Increase	Decrease	No Change
Formation of Adhesions								
No treatment	115	89	77%					
Heparin in saline (2 doses)	21	15	71%					
Heparin in Pitkin's menstruum (1 dose)	5	3	*					
Reformation of Adhesions								
No treatment	18	17	94%	7 cm	9 cm	10	8	0
Heparin in saline (72 hours)	20	17	85%	8 cm	6 cm	10	8	2
Heparin in Pitkin's menstruum (72 hours)	21	19	90%	8 cm	6 cm	6	11	4
Heparin in Pitkin's menstruum (1 dose)	4	4	'	9 cm	13 cm	3	1	0
Saline alone	5	4	'	8 cm	5 cm	2	3	0
Gelatin 5% aqueous solution	6	5	'	7 cm	6 cm	3	3	0

\* Series not large enough to warrant percentage

**DISCUSSION**—The summary in Table I demonstrates that the likelihood of developing adhesions was almost as great in the rabbits treated by heparin as in those that were not treated, or were treated by saline or gelatin. There was no significant difference in the average extent of involvement of bowel by adhesions or in the numbers of rabbits that had an increase or a decrease in the amount of adhesions.

It has been suggested by Lehman and Boys,<sup>9, 10</sup> and others, that heparin might prevent or minimize the formation of fibrin and the development of adhesions. Our histologic studies in rabbits dying of hemorrhage during heparinization revealed fibrinous exudate or fibrin at the site of injury.

Although Brunn,<sup>15</sup> Clarke,<sup>16</sup> and Heitzler<sup>17</sup> have studied regeneration of mesothelium, there is no definite evidence determining the rate of growth. Mesothelium has been described as originating from the edges of defects or as developing by a differentiation of connective tissue cells (Baily<sup>18</sup>). Since

young mesothelial cells are easily lost in preparation of tissue for microscopic study and since it is difficult to differentiate mesothelial cells from flattened wandering cells in cross-section preparations, our histologic studies have not solved these problems with certainty. It seemed, however, that reperitonealization may require a period of time longer than the maximum of 72 hours used for treatment in these and other experiments.

### CONCLUSIONS

1 Heparin in large doses, continued up to 72 hours, has not prevented the formation or reformation of intraperitoneal adhesions or the deposition of fibrin on the surface of injured appendices in rabbits.

2 There was a spontaneous failure of development of adhesions in 23 per cent of the rabbits used in this experiment. There were also 6 per cent of the rabbits subjected to division of adhesions, and no other treatment, that did not redevelop adhesions. Heparin increased the likelihood of not developing adhesions by less than 8 per cent.

3 The extent of the adhesions that redeveloped after division and heparinization was equal to that observed in control experiments.

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# THE QUESTION OF REGENERATION OF NERVE FIBERS TO THE HUMAN ADRENAL GLAND AFTER BILATERAL SYMPATHECTOMY\*

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THE INEFFICACY of the medical treatment of hypertension was the prelude to the search for other, more potent means, of dealing with this widespread and inevitably fatal disease. In 1924, N Pende presented before the Congress of Internal Medicine, at Padua, his conception of a surgical procedure based upon the observation that resection of the left splanchnic nerve resulted in an atrophy of the adrenal gland and a diminution of the secretion of epinephrine. From then on, this addition to the therapeutic arsenal was developed and perfected by Leriche and Wertheimer, in France, and Peet, Smithwick, and others, in this country. Its physiologic basis is yet to be established, and the procedure itself has frequently been criticized because of the reported regeneration after experimental sympathectomy in animals. In man, Rogoff<sup>1</sup> has reported a case of Addison's disease following sympathectomy.

The statement has been made several times<sup>2, 3</sup> that the present-day sympathectomy for hypertension completely denervates the adrenal glands. Insofar as I know, this has never been proven in the human. Smithwick<sup>4</sup> has ascribed the rise in blood pressure in the weeks following sympathectomy to the "regeneration of the interrupted vasoconstrictor pathways." To my knowledge, its actual demonstration in man has never been undertaken. If regeneration of these resected nerve fibers occurs, one might demonstrate this in an end-organ, such as the adrenal gland. The anatomic method was selected as a means of approach, and, therefore, a study was undertaken to determine the extent, if any, of regeneration of sympathetic nerve fibers to the human adrenal gland following bilateral sympathectomy.

The innervation of the human adrenal gland is still not completely understood, perhaps largely for technical reasons. In 1944, I made a comprehensive study of the innervation of the normal adrenal gland of man, and other forms. The adrenals of man receive their innervation through the greater and lesser splanchnics and from the neighboring ganglia. This innervation is mostly preganglionic, with some postganglionic fibers coming from the solar plexus. The presence of numerous ganglion cells in the human medulla would indicate the presence of an additional postganglionic innervation.<sup>5</sup> From this brief review, one may draw a working hypothesis that bilateral splanchnicectomy and thoracolumbar sympathectomy should produce a complete degeneration of the preganglionic fibers of the gland, with only the postganglionic fibers remaining. The effect on the ganglion cells would remain to be determined.

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\* Read before the New York Pathologic Society, April 25, 1946

The anatomic and physiologic experimental evidence has, for the most part, been contradictory, partly the result of failure to interpret differences in species and partly due to variations in experimental technic. Elliott,<sup>11</sup> Hollinshead,<sup>12</sup> Swinyard,<sup>13</sup> and Young,<sup>14</sup> in the cat, have shown that the innervation of the chromaffin tissue is preganglionic with few or no postganglionic fibers. In my own experiments on the rabbit, the fibers of the adrenal were almost completely degenerated seven days after infradiaphragmatic splanchnic resection. However, I also found some crossed innervation, this may be peculiar to rabbits. From an anatomic standpoint, Hollinshead and Finkelshtein<sup>15</sup> showed that regeneration to the ipsilateral gland occurred in cats following unilateral sympathectomy and splanchnicectomy as early as the 2nd month, and at the 5th month an apparently normal innervation existed.

Bacq and Dworkin<sup>16</sup> in two of three cats, one year after total bilateral sympathectomy, found physiologic as well as anatomic evidence of regrowth of preganglionic fibers. Hodes,<sup>17</sup> working in Cannon's laboratory, found that 30 days after sympathectomy physiologic evidence seemed to point to a regrowth of fibers to the adrenal medulla. This author wisely pointed out the possibility of the intervention of other fibers in his experimental results. Haimovici and Hodes<sup>18</sup> performed a total sympathectomy upon seven cats. Their physiologic criteria indicated sympathetic regrowth in all animals. They emphasized that in order to keep regeneration at a minimum the greatest possible preganglionic destruction should be carried out. Maes and Simeone,<sup>19</sup> working with cats, crushed the splanchnics in the chest and beneath the diaphragm. From the degree of physiologic response they concluded that regrowth of fibers must be considered six weeks after operation. In all of these physiologic studies, anatomic data were lacking, or inconclusive.

Numerous experiments on dogs by Hermann, and his school,<sup>20, 21, 22</sup> in France, have suggested that the endocrine elements show no morphologic changes following complete sympathectomy, and that minimal amounts of epinephrine were still present.

Of the more recent papers, that of Papez, Jensen, and Dukes<sup>23</sup> is enlightening. Two years after complete sympathectomy in dogs, they found only a minimal amount of regeneration, not in excess of 5 per cent. There were some postganglionic fibers coming from the neighboring ganglia which were not affected by the operation. In addition, they found a few end-bulbs, and thickened endings in the medulla.

#### CLINICAL SUMMARIES

**Case 1**—E. B., a 45-year-old white male gave a three-year history of dyspnea on exertion, dizziness, headaches, and failing vision, all becoming more marked in the few weeks before admission. Physical examination showed a blood pressure of 260/155, with an enlarged heart and slightly enlarged liver. The eye grounds were typical of severe hypertensive retinopathy. The urine contained two plus albumin, with a few red cells and rare white blood cells. Kidney function tests were within normal limits. The electrocardiogram was suggestive of myocardial damage.

Right sympathectomy on 11/19/43. The greater and lesser splanchnics from T8 down to, and including, the semilunar ganglion, as well as the sympathetic trunk from

T 8 to L 2 were removed. Many of the branches of sympathetic chain were excised as well. Left sympathectomy was done on 12/3/43, the operation was the same as on the right side.

**Pathologic Report** Fragments of nerve and ganglia without significant change.

The postoperative blood pressure was 180/120, with pronounced orthostatic hypotension. Postoperative recovery was uneventful. On June 15, 1945, the patient was admitted to the New York City Hospital for recurrence of symptoms of a four-month duration. The blood pressure was 235/140 and rose at one time during his stay to 255/140. His course was downhill, and he died August 13, 1945 in uremic coma (NPN-210), 195 months after operation. The postmortem done five and one-half hours after death, showed pulmonary edema, cardiac hypertrophy, bilateral chronic adhesive pleuritis, and arteriolar nephrosclerosis.

**Case 2—S R** This was a 50-year-old white male, with a three-year history of convulsive seizures, syncope, and severe headaches. The blood pressure varied from 180/100 to 210/110. The heart was enlarged, and the electrocardiogram showed moderate myocardial damage. The urine contained one plus albumin, and showed some white blood cells. The kidney function tests were normal. Spinal tap was negative. The diagnosis of hypertensive encephalopathy with essential hypertension was made and sympathectomy was advised.

Right sympathectomy on 5/31/45. The sympathetic trunk from T 9 to L 2, as well as all communicating branches were resected. The greater and lesser splanchnics were isolated from T 6 down to, but not including, the semilunar ganglion, cut, and excised. Left sympathectomy was done on 6/18/45, the same procedure was repeated.

**Pathologic Report** The nerves and ganglia showed some changes, which, however, are within normal limits.

Postoperatively, the blood pressure dropped to 170/100, and recovery was without incident. However, the symptoms remained, and the blood pressure rose rapidly to the preoperative levels. The patient died on January 15, 1946, seven months after operation. The autopsy done 36 hours after death, showed subdural hemorrhage, cardiac hypertrophy, moderate coronary sclerosis, and arterial as well as arteriolar nephrosclerosis.

Clinically, sympathectomy was undertaken in each case with the hope of arresting the advance of the disease. In both cases, the blood pressure reached the preoperative level before death. It is of interest to note that the pathologic report of the resected nerves and ganglia was essentially negative. Studies, which Dr J A Lisa and I have undertaken of this material, using various staining methods, seem to indicate that there is some deviation from the normal in the splanchnic nerves and sympathetic ganglia removed from hypertensive patients at operation. Whether this is a primary phenomenon or secondary to the generalized arteriolar disease, from which many of these patients suffer, remains to be determined.

#### MATERIALS AND METHODS

Slices of an average width of two to three millimeters were taken from each gland and impregnated with silver, according to the method of A Weber<sup>8,9</sup>. Serial sections were made of the totality of each slice, at ten micra per section, all sections were examined. This method permits tracing the exact distribution of nerve fibers as they enter the adrenal gland, as well as an accurate study of the ganglion cells. It is probable that frequent errors in the quantitative study of ganglion cells in the human adrenal are due to methods where serial sections are made and only one in every five or ten are

examined. Thus, one can see why ganglion cells, having a thickness of only 10 to 20 micra can easily be missed, or thought to exist in small numbers only. Many fields were examined under high power and oil immersion. Adrenals coming from patients who had not undergone sympathectomy served as controls, and these slices were processed in the same batches as the other material.

### OBSERVATIONS

Before describing my own results, it is necessary to say that the use of silver stains allows one to distinguish between pre- and postganglionic fibers. This has been demonstrated anatomically by Weber,<sup>8</sup> and Nonidez and Hare.<sup>24</sup> In the sections the preganglionic fibers are dark brown, and the postganglionic fibers are light brown.

The first very striking observation in the two cases of this study was the almost complete absence of nerves in the medulla. The usual picture of interlacing and branching fibers, or fine fibrils, found in the sections of normal adrenal medulla was not seen. Occasionally, a few very fine fibrils were encountered, and, here and there, a nerve trunk. Otherwise, search of field after field revealed no nerves (Figs 1 and 2). The fibers that were present were almost entirely light brown, therefore, postganglionic, and only rarely was a preganglionic fibril noted. At places where the nerve trunks were traced into the cortex and medulla, wide spaces were apparent between the pale brown fibrils, corresponding, without doubt, to the absent preganglionic fibrils (Figs 3 and 4). In most instances the remaining nerves entered the gland together with blood vessels. They pass through the cortex and eventually break up to distribute themselves in the medulla. There, fine postganglionic nerve endings were encountered on the walls of the vessels.

Ganglion cells can be found in the normal adrenal of man in three places: in the ganglia of the capsule, in nerves as they pass through the cortex and medulla, and in the medulla.<sup>5</sup> They are usually in groups, but may be found isolated or in the path of a fiber. Their intensely-stained cytoplasm, with a large pale nucleus and numerous dendritic processes make them easily identifiable (Fig 1). The dense intercellular plexus formed by the branching of the arriving preganglionic fibers is very striking. They form synaptic endings on the ganglion cell itself.

After sympathectomy the picture is quite different. In both cases the numerous dark interlacing preganglionic fibers are absent, and the ganglion cells look peculiarly isolated, nevertheless, retaining their normal characteristics (Fig 2). Their argyrophilia, however, seems to be slightly diminished. Other findings of a more morphologic nature, such as swellings of nerve endings, or nerve fibers, and rarity of giant nerve endings have been briefly reported elsewhere.<sup>6</sup>

**DISCUSSION**—It is obvious that in these two cases there has been virtually no regeneration of the nerve fibers in the adrenal gland. What is the nature of the remaining fibers in the medulla? The postganglionic fibers in any case would not have been directly affected by the operation. However, the presence



FIG 1

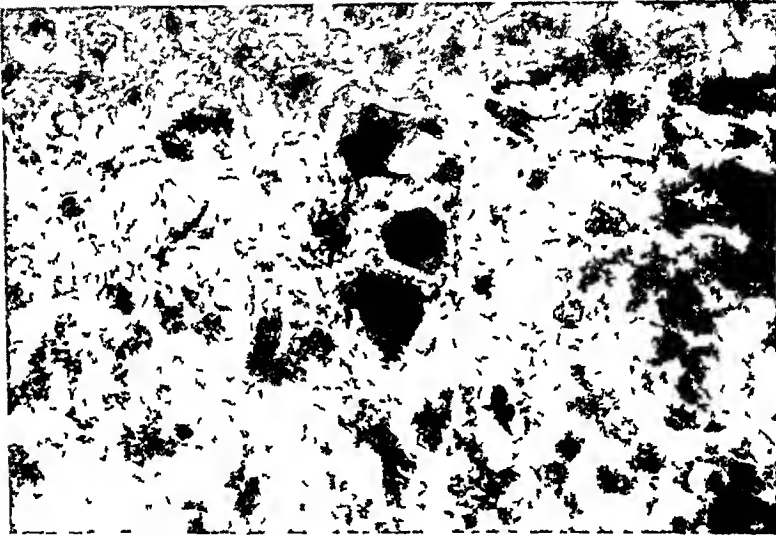
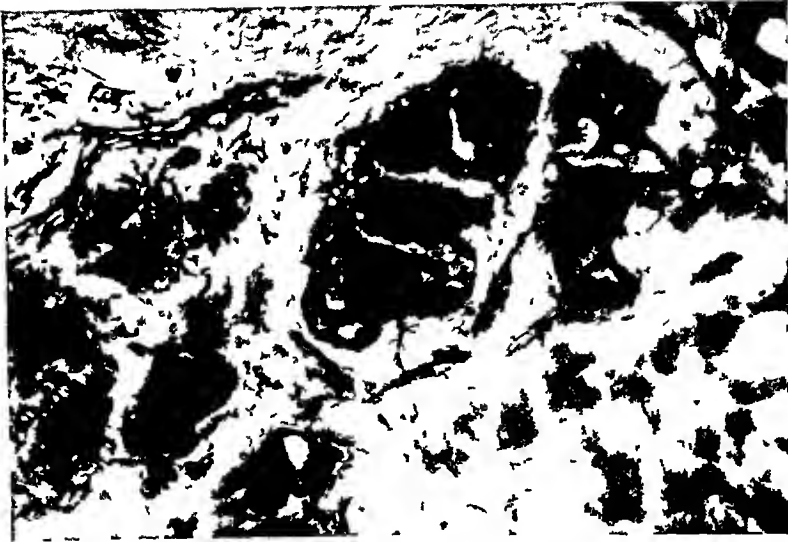


FIG 2

FIG 1—Normal adrenal gland (control)

Ganglion cells with dark brown preganglionic fibers. A nerve trunk is in the upper left, and the medulla at the lower right, fine nerve fibrils are visible in the latter. The somewhat separate-appearing round area at the right upper margin of the uppermost of the group of four ganglion cells is a giant nerve ending ( $\times 95$ )

All sections are 10-micra thick, and stained according to the Weber silver technic

FIG 2—Adrenal after bilateral sympathectomy

Group of pale ganglion cells in the medulla. The interlacing plexus of preganglionic fibers has all but disappeared, and the surrounding medulla is devoid of fibers ( $\times 160$ )

of the very few dark brown preganglionic fibers raises the question as to whether they are regenerated fibers or are fibers which have escaped degeneration. In their experiments on dogs, Papez, and his co-workers, felt that the

FIG 3

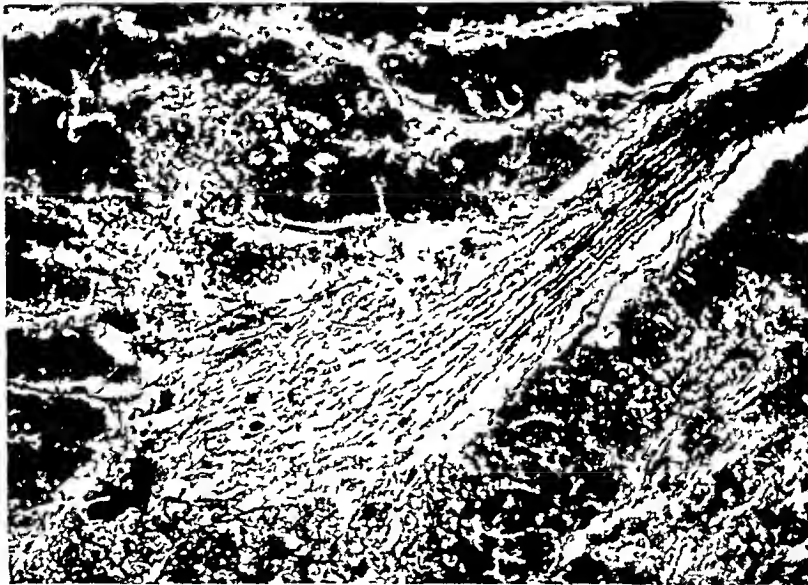
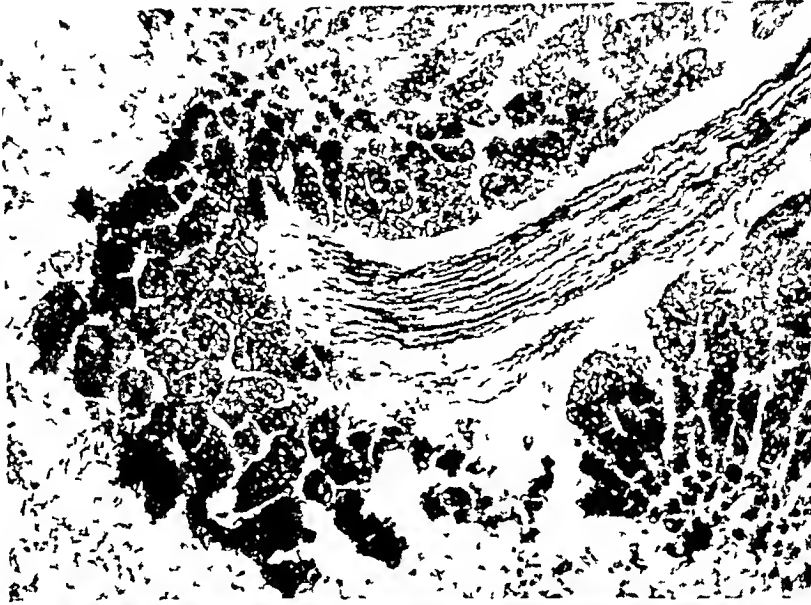


FIG 4

FIG 3—Normal adrenal gland (control)  
Nerve trunk composed of preganglionic fibers passing through the cortex towards the medulla ( $\times 360$ )

FIG 4—Adrenal after bilateral sympathectomy  
The preganglionic fibers have disappeared and one sees only the more pale-staining postganglionic fibers ( $\times 360$ )

number of normal fibers seen in the adrenal medulla two years after operation did not exceed those of the recently subtotally sympathectomized dog. They stated, however, that these were probably postganglionic fibers. My own obser-

vations based on staining differences between pre- and postganglionic fibers indicate that some of the remaining fibers are certainly preganglionic. It would seem that these are fibers which have escaped degeneration.

From a theoretic standpoint, the extent of the resection in these two cases makes regeneration over such a wide distance a very questionable occurrence. As Weber<sup>10</sup> has shown, even when the two cut-ends of a nerve fiber lie within a short distance of each other, their reunion is a matter of chance. In addition, he states "The greater the distance between the cut-stumps of the nerves, the greater the phenomena of negative neurotaxis." Experimental evidence by Papez, and his group, indicates that after two years "the regeneration of splanchnic and sympathetic nerves after total sympathectomy is relatively small, and far smaller within the gland than suggested by the size of the regenerated false nerve trunks when no histologic examination is made." They also stated that "the process of regeneration of nerve fibers to the gland seemed to be fortuitous, variable, and at best very scanty." The study of my two human cases is in accord with their microscopic observations on dog adrenals.

Rogoff's contention, in his widely cited paper,<sup>1</sup> that "denervation of the gland by section of its nerves is usually followed by regeneration of the nerve supply within a few weeks" is contradicted by the observations of this study. It would be more logical to assume that the Addison's disease in his report was the result of interruption of the vascular supply to the gland. Besides, only the deepest layers of the reticular zone are innervated.<sup>5</sup>

The absence of degeneration of the ganglion cells lends support to the synaptic theory of nerve conduction. The normal histologic picture of the secretory elements of the adrenals of both cases confirms the findings of previous investigators<sup>21, 22, 23</sup>. Unpublished observations indicate that this is not altogether the case in the first days after sympathectomy.<sup>7</sup> The rarity of giant nerve endings, which are a constant occurrence in the normal adrenal medulla of man, leads one to suspect that they are endings of preganglionic nerve fibers.

#### CONCLUSIONS

(1) In two cases of human hypertension, following extensive bilateral sympathectomy, there were only a few nerve fibers left in the adrenal glands. These were mostly postganglionic fibers.

(2) The postoperative return to hypertensive levels of the blood pressure following sympathectomy cannot be explained by regeneration of nerve fibers into the adrenal gland.

I am deeply indebted to Dr J. A. Lisa, Pathologist to the New York City Hospital and Doctor's Hospital, New York, who provided me with most of the material upon which this paper is based.

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## RETROPERITONEAL CYSTS

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RETROPERITONEAL CYSTS have been defined by Handfield Jones<sup>10</sup> as those cysts lying in the retroperitoneal fatty tissues which have no connection with any adult anatomic structure save by areolar tissue. The rarity of retroperitoneal cysts, the speculation as to their exact origin and the uncertainty of their diagnosis makes them among the most interesting of all abdominal tumors. While a good many isolated case reports of these cysts of one type or another appear in the literature, there is an apparent lack of unanimity among various authors as to the origin of these cysts. The case report herewith appended is a rather typical one, in which the diagnosis was made preoperatively.

**Case Report**—Miss M. B., a white female, age 26, was first seen on January 21, 1944, at which time she complained of soreness and a lump in the right lower abdomen. The patient does not remember having symptoms until about November, 1943, when she first had soreness occasionally across her lower abdomen. She thinks she has had vague pains for three or four years, but she did not feel the lump there until this time. There has been no weight loss and no change in bowel habits, no change in periods. Wearing tight garments across the waist causes some discomfort. There is no change in the tumor with the menstrual cycle or with gastro-intestinal or urinary functions. She thinks the tumor has very gradually grown a little larger. The past history and review by systems was not pertinent.

Physical examination revealed a tall, thin girl, appearing quite healthy, with normal pulse, temperature, and a blood pressure of 100/80. The head, neck and chest were normal. In the right lower quadrant of the abdomen, there is a cystic-feeling tumor mass which is nontender, or only slightly so, slightly movable, does not apparently reach the anterior abdominal wall and lies above the brim of the pelvis. The right kidney is just palpable to deep palpation and is not tender. The left kidney, liver, gallbladder and spleen are not palpably enlarged or tender. Pelvic examination reveals no palpable abnormalities, the mass lies above pelvic palpation. Hematology on January 24, 1944: Hemoglobin 100 per cent, RBC 4.8 million, WBC 7300, PMN 73, SL 22, monocytes 4, Kolmer and Kahn negative. Urinalysis, SG 1005, albumin 0, sugar 0, casts 0, pus 0, red cells 0. Barium enema of the colon showed that it filled readily and presented no evidence of intrinsic organic lesion. The palpable mass in the right lower quadrant of the abdomen produces a compression and displacement deformity of the distal limb of the hepatic flexure and of the right side of the transverse colon, these segments of the colon are quite firmly attached to the mass, and this portion of the colon takes a course around the lower margin of the mass. Palpation elicits no tenderness over the colon or in the region of the palpable mass. The terminal ileum and appendix are not filled during the period of fluoroscopy. Retrograde pyelogram. Opaque material injected through catheters inserted into both ureters demonstrates normal outlines of the left calices, renal pelvis and ureter. The left kidney outline is normal in size, shape and position. The right kidney is normal in size, it occupies a low and rotated position and there is a moderate right pyelectasis. The right ureter is deviated sharply toward the left, the apex of this displacement curve is at the level of the lumbosacral joint and in this segment, the ureter deviation is evidently produced by the same palpable mass which produces displacement of the colon, in the previous barium enema examination. *Clinical Diagnosis* Retroperitoneal cyst.

## RETROPERITONEAL CYSTS

*Operation*—A long right rectus incision disclosed a cyst which lay behind the terminal ileum and cecum and which had displaced the ureter medially and the cecum laterally and anteriorly (Fig 1) The gallbladder, appendix and the pelvic organs were normal The transverse colon was adherent to the cystic mass The posterior peritoneum was divided lateral to the cecum and transversely below the terminal ileum for a distance of about five inches The cyst, which was about the size of a grapefruit, then presented By combination of sharp and blunt dissection, applying hemostats to the cut peritoneal edge for traction, it was possible to enucleate the cyst and it was not ruptured until almost completely removed (Fig 2) It was filled with clear, brownish-yellow fluid Bleeders were stopped by packing and ligature The appendix was then removed, and the abdomen closed The convalescence was uneventful



FIG 1—Appearance of cyst after retracting transverse colon

*Pathologic Examination—Microscopic* Dr John D McGovern Multiple sections through the thickened area in the cyst reveals in one area a diffuse irregular anastomosing series of tiny cleft-like and well-formed channels lined by typical endothelial cells Scattered foci of lymphocytes and monocytes are interspersed throughout this area and the large cyst The lining is composed for the most part of a well-defined zone of collagenous connective tissue interspersed with irregular short bundles of a more deeply eosinophilic-staining material tending to produce elongated convolutional stria-like forms in the wall At one point in the section the cyst is in direct continuity with a large area of typical angioma and the vessels contain occasional blood cells as well as precipitated lymph but the majority of the channels are truly without content *Pathologic Diagnosis* Retroperitoneal massive cystic lymphangioma

This case is rather typical in that the patient was an adult female, the tumor was on the right side, the history and physical findings were characteristic, the size of the mass is about that usually encountered in previous case reports, and roentgenologic studies presented the characteristic appearances Comparing this case with other case reports in the literature it might almost

be stated that this condition represents a fairly well-defined clinical entity as far as the history, signs, symptoms and treatment are concerned. The difficulty arises when one attempts to classify these cysts embryologically and to ascertain their incidence statistically by type.

Handfield Jones, whose article on this subject is the most widely quoted, and is generally regarded as a classic, gives the following classes of cysts (I have changed his order to fit this paper)

- (1) Cysts of urogenital origin
- (2) Teratomatous or dermoid cysts
- (3) Lymphatic cysts
- (4) Cysts of mesocolic origin
- (5) Traumatic blood cysts
- (6) Paracystic cysts
- (7) Developmental cysts in full formed kidney or pancreas

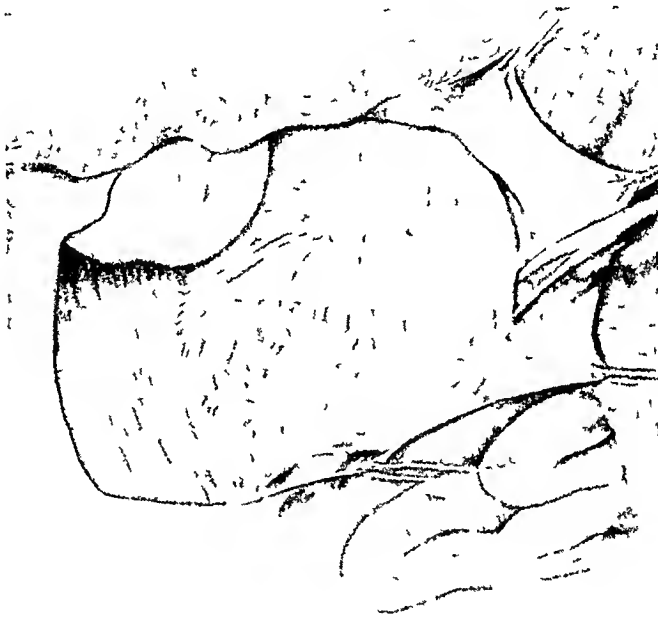


FIG 2—Dissection of cyst half completed, ureter being freed

On the last three classes of cysts this paper has no comment and Handfield Jones mentions them simply as of interest from the diagnostic point.

Standard pathology texts<sup>16</sup> give the incidence of cystic retroperitoneal tumors as being much lower than solid retroperitoneal tumors. Kretschmer and Hibbs<sup>17</sup> quote Gobell's<sup>8</sup> 1901 collected report of 101 retroperitoneal tumors of which 12 were retroperitoneal cysts. Frank<sup>5</sup> reviewed the literature between 1925 and 1936 and collected 107 cases of which eight were cysts. These included two lymphangiomas, two lymph cysts, two sanguineous cysts, one serous cyst and one hemangio-endothelioma (all recovered). The majority of these tumors were mesodermal in origin. There were also ten teratomas in his list, of which five recovered. Concerning the relative frequency of retroperi-



FIG 3A —Low power photomicrograph of cyst wall (Thickest area)

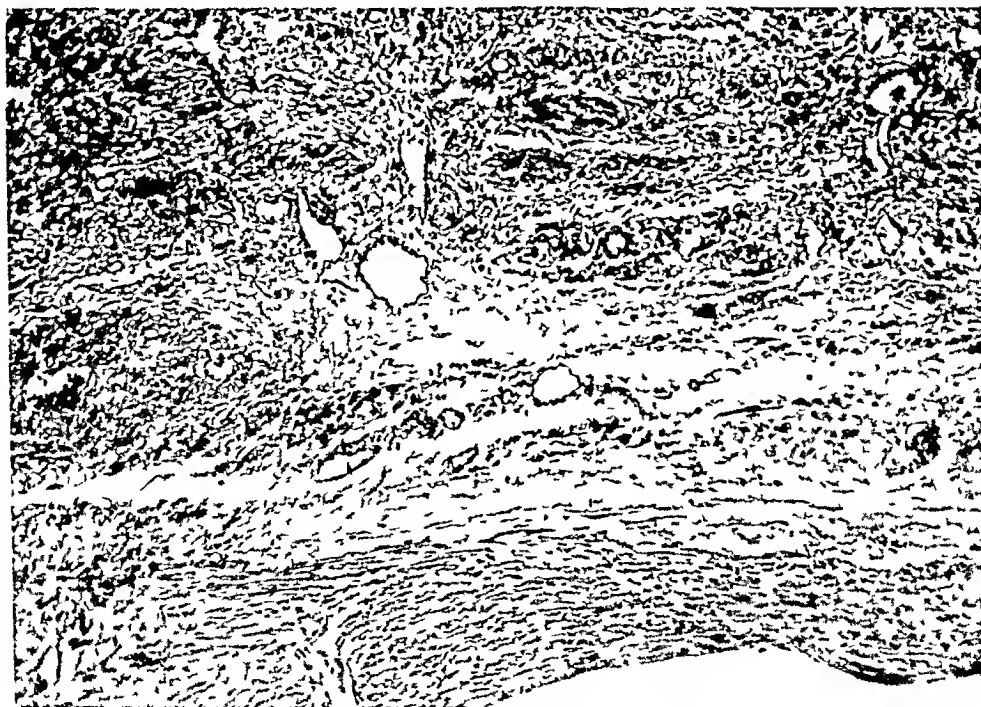


FIG 3B —Medium power photomicrograph of cyst wall (Thickest area)



toneal *versus* mesenteric and omental cysts, Geister<sup>7</sup> states that there are between 450 and 500 case reports on the latter and only 18 on the former

According to Hinman, Gibson and Kutzmann<sup>1</sup>, nearly all cystic retroperitoneal tumors have their origin from fetal renal elements. This view is supported by Maury,<sup>22</sup> and by Jacquot and Fairise.<sup>15</sup> Maury's case had tubules and glomeruli in the wall and a ureter-like tubular structure attached to it. Jacquot and Fairise' case also had recognizable renal elements in its wall and was situated between the layers of the descending mesocolon. This type of cyst was first described by Roth<sup>20</sup> in 1881. Hinman, *et al*, state that "it is highly probable that a great variety of cystic and solid neoplasms of the retroperitoneal

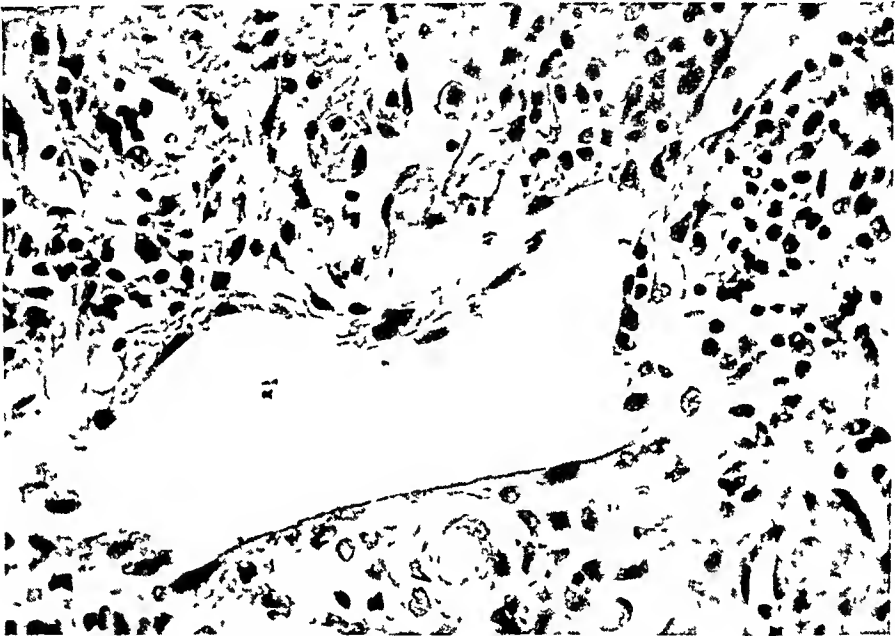


FIG 3C—High power photomicrograph of cyst wall (Thickest area)

space in relation to the adrenal, kidney, broad ligament, spermatic cord, epididymis and possibly the testicle have their origin in wolffian body remnants." In support of this theory is the frequency of the condition in women where the mullerian duct makes up the generative tract and the wolffian body exists almost entirely as an atrophic unutilized condition. On the other hand, Hinman, *et al*, quoting Maury, state that only five cases with primitive glomeruli and renal tubules in the wall are reported in the American literature. Their assumption is that the variety of findings, microscopically, in the wall of the cyst is due to the neoplasm arising out of one of the many portions of the wolffian body.

Closely related to cysts of wolffian body origin, and often considered as of the same type, are cysts arising from the cells of the genital ridge which lies just lateral to the wolffian body. These cysts, when characteristic, assume the

appearance presented by Stewart's<sup>27</sup> case, which was described as a unilocular compound cystic ovarian adenoma, four and one-half inches in diameter, situated on the outer side of the ascending colon. Stewart's conjecture poses the possibility that these cysts are distant relatives of retroperitoneal teratomas and dermoids of the ovary, the common ancestor being a totipotential sex cell which becomes sequestered on its course from the morula to the genital ridge and later in adult life assumes independent growth qualities.

This view is more or less accepted by Lahey and Eckerson<sup>18</sup> who reported two cases of this type in 1934. They state that "mesenteric, omental, and retroperitoneal cysts must actually be grouped in the same category since the mesenteric or omental variety are merely an anterior extensive or inclusion of those originally retroperitoneal." The distinction, they go on to point out, is based on clinical signs while pathologically and embryologically, the cysts are alike. They suggest that since the cysts spring from one of the three germinal layers, those from the ectodermal and endodermal elements may be classed as dermoids and those of mesodermal origin called mesodermoids. Of Lahey and Eckerson's two cases, one was retrocecal and no microscopic report is appended. The other was reported as a simple cyst of the ovary and lay lateral to the descending colon.

Typical retroperitoneal teratomas are, as noted in Frank's review of the literature, at least as common as all other retroperitoneal cysts put together, but retroperitoneal dermoids are less common. Handfield Jones includes three cases in his review, these usually contained sebaceous material and hair.

Although there are a number of cases of chylous and nondescript lymphatic cysts reported in the literature, there are, or were according to Kretschmer and Hibbs, only five cases of typical retroperitoneal lymphangiomas, all on the right side, reported up to 1934 (two children and three adults). The view is supported by Ingraham and Nelson<sup>14</sup> who, in 1939, reported the case of a woman with a large cystic midline lymphangioma of the retroperitoneal space. They consider their case to be the sixth in the literature. While these authors quote McFadden,<sup>25</sup> and Makins,<sup>21</sup> as being of the opinion that many of the reported mesenteric and retroperitoneal cysts are lymphangiomas, they prefer not to accept this opinion.

Unfortunately, many of the earlier reports on so-called "chyle cysts" were based on the finding of a milky contents within these cysts rather than in accurate study of the cyst wall. Gerster, who made an extensive study of this subject, points out that chyle and lymph are indistinguishable grossly, and that studies of the fat content from lymph fistulae from the lower extremities have shown variations almost identical with chyle itself (from 0.6 to 47 per cent). He also quotes Volkmann<sup>20</sup> as having observed a chyle-containing cystic lymphangioma in the neck.

Hadley,<sup>9</sup> in 1916 pointed out that retroperitoneal lymphatic or chylous cysts are probably related to hygromata in the neck and are derived from one of the four primitive lymphatic sacs. The principal objection to this theory is that most of the abdominal cystic lymphangiomata reported have been in adults.

while most hygromata of the neck are in children. In favor of this condition being a separate entity from wolffian body cysts is that the reported cases occur almost as often in males as females and while some of these cysts may be indistinguishable from some of the wolffian variety, some, at least, have quite definite characteristics of their own. A typical cystic lymphangioma has walls composed of connective tissue with numerous endothelial-lined lymph spaces which in some areas show cavernous development. Besides connective tissue, smooth muscle cells are present and more or less lymphoid infiltration. The cyst may have an endothelial lining or it may be absent. The contents may be serous or chylous and bloody if traumatized. No connection with nearby lymphatics is necessary.

Some of these cysts apparently arise from degenerating or regressive changes in cavernous lymphangiomas. Since Gerster's report, another case has been reported in 1942 by Lee.<sup>20</sup> Lee presents an ingenious hypothesis for the origin of chylous cysts. On the basis of a small effusion following trauma there is an ingrowth of endothelial cells and a cyst is formed by a reversed flow of chyle into this space.

TABLE 1

ADDITIONAL CASE REPORTS NOT PREVIOUSLY SUMMARIZED

Author	Sex	Age	Type	Size	Location
1 Barthels <sup>3</sup>	F	44	Lymphatic	Child's fist	Midline
2 Corniologu <sup>4</sup>	F	35	Parchment thin wall lined with calciform cells	Infant's head	Retrocecal
3 Forster <sup>5</sup>	F	36	Wolffian type lined columnar epithelium	Diameter 12-15 cm	Connected to left kidney
4 Lawen & Biebl <sup>18</sup>	F	18	Wolffian type with glomeruli in wall	30 cm long	Attached to right renal vessels
5 Rosenfeld <sup>26</sup>	F	28	Exceedingly thin lining isolated epithelial cells and leukocytes	Goose egg	Retrosigmoidal

Handfield Jones distinguishes another type of cyst, which he calls mesocolic in origin, formed by imperfect fusion of the layers of the peritoneum. This cyst is found only in the area between the ascending and descending colon and below the transverse mesocolon and it always lies anterior to the spermatic or ovarian vessels. These cysts have a thin fibrous wall and a delicate flattened lining. He describes one case of this type which "is either mesocolic or lymphatic in origin." In perusing the literature, I have been unable to find any recorded cases which fulfilled these characteristics unless it be that of Wilson,<sup>32</sup> described in 1929, and Wilson is quite doubtful about the origin in his case.

From the foregoing review it seems apparent that there are actually two general types of primary developmental retroperitoneal cysts, the distinction between the two being as follows. One type is that derived from ectodermal (or perhaps of entodermal) elements, the wolffian body or genital ridge or a more primitive cell, and shows in its wall epithelial elements. This cyst usually occurs in women and occupies a lateral position. The second type is derived from mesodermal, or lymphatic elements and occurs in any age-group and either sex, and may have either a midline or a lateral position. As to the

incidence of either one of these types of cysts, one can only speculate. In addition to the 18 or 20 cases of lymph cysts collected by Gerster and the five wolffian body cysts reported by Hinman, *et al*, there are Lahey's and Eckerson's two cases and others mentioned here, and I have been able to find at least three more wolffian types and two lymphatic in the literature not recorded in these summaries (Table I). Incomplete references to the incidence of this condition are common. Hinman, *et al*, state "the literature abounds with reports of cysts which are considered as being of wolffian origin—" Whipple,<sup>31</sup> discussing Gerster's paper, infers that he has had several cases. Barney,<sup>1</sup> in 1925, was able to find five cases in the records of the Massachusetts General Hospital and makes the statement that the tumors are more frequent in women than men. Stone,<sup>28</sup> discussing Barney's paper, remarks that he has had three or four cases in children. Hawthorne<sup>12</sup> stated that he had operated upon two patients for retroperitoneal cysts.

Regardless of their origin, the walls of these cysts are usually described as having three layers, microscopically. An outer connective tissue layer, a middle lymphoid layer, and an inner layer lined with flattened cells. At times these cells may assume columnar form and at other times they are so flattened as to be absent or endothelial in character. The presence of ovarian elements, adenomas or malignancies, skin, hair or lymphoid elements, *etc*, is necessary to make an exact diagnosis. Except for dermoid types and cysts which have undergone inflammatory or malignant changes, the walls are so thin that they are often ruptured on removal. Most of the reported cases have, like the author's case, been found on the right side, that is retroceally rather than retrosigmoidally.

The general group of symptoms noted in all these tumors is that of inconvenience, discomfort and pressure, incident to size. As a rule they are painless because they are slow growing and the function of adjacent structures is not impaired. General or local enlargement of the abdomen in conjunction with a feeling of discomfort is the most usual complaint. Other symptoms include anorexia, pain and dyspnea, all noted in the larger-sized tumors accompanied by weight loss. Infection occurring in these cysts is apparently of unusual occurrence, and presents the signs of local tumor with sepsis and severe pain.

The diagnosis of retroperitoneal cysts is made by a process of eliminating other possible tumors. The importance of pyelography and the barium enema in the diagnosis of retroperitoneal cysts has been pointed out by Lahey, *et al*. By these procedures, the correct diagnosis was made in the first case reported. The condition is to be suspected in a patient who has an asymptomatic, rounded, rather immovable cystic-feeling tumor in the right or left lateral abdomen. Disease of the kidneys, ureter or colon is ruled out roentgenologically, mesenteric cyst, according to Moynihan,<sup>24</sup> is generally near the umbilicus and very mobile, pancreatic cysts present in the upper abdomen and lie behind the transverse colon until quite large, and roentgenograms of the duodenum show elongation of the duodenal loop. Cysts arising from the adrenal, kidney, pan-

cysts of the intestine are always to be ruled out in the differential diagnosis. Although these are also retroperitoneal cysts, they are not to be confused with the true primary retroperitoneal cysts under consideration above. A retroperitoneal cyst may also simulate a high-lying ovarian cyst, and be so diagnosed preoperatively.

The treatment of this condition is entirely surgical and the uncomplicated cyst becomes a problem to the surgeon only because of its intimate relation to the great vessels and the ureter. By making a vertical incision in the peritoneum lateral to the cecum and extending this transversely across the brim of the pelvis and displacing the colon upward as well as medially, one can approach the ureter and great vessels and keep them under direct visualization during the process of removing the cyst. A little care in handling the mesentery of the bowel prevents any bleeding and, providing the field is kept dry, no difficulty should be encountered in avoiding the ureter and the great vessels. The cysts have a tendency to rupture during removal as the walls are very thin. This accident has no effect on the outcome of the operation but makes it more difficult to determine whether the entire cyst has been removed or not. Occasionally, marsupialization of the cyst wall may be necessary in cases in which the patient is a poor surgical risk or in complicated cases. This procedure will effect a cure in a chylous cyst.

The prognosis with removal of these cysts is excellent. Occasionally the cystadenomas undergo malignant changes, and Harrington and Ganshorn<sup>11</sup> report a case of a malignant cystic hemaigio-endothelioma lying retroperitoneally, resulting in death of the patient.

#### SUMMARY

A discussion of the various theories for the origin of primary retroperitoneal cysts has been given, together with the accepted methods of diagnosis, treatment and a report of a personal case.

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# A STUDY OF THE RESULTS OF THE SURGICAL TREATMENT OF VARICOSE VEINS

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DESPITE the many recent reports concerning the surgical treatment of varicose veins, it is difficult to find large series in which end-results after an adequate period of follow-up are given. Even more unusual are groups of cases in which comparisons are made between various types of operative procedure employed under similar conditions. Among the many competent and experienced authors there seems to be no general agreement on the operation offering the best chance of a cure of this very common disorder.

In 1942, Moore and Knapp<sup>1</sup> reviewed 121 cases of varicose veins from the Surgical Department of the New York Hospital. We present a reconsideration of their findings on the basis of a larger series of cases and, in addition, a study of factors which they did not discuss. To accomplish this we have reviewed all cases of varicose veins treated by operation between 1940 and 1944, to obtain information concerning physical findings, the type of operation employed, duration of hospitalization, number of postoperative injections required to give satisfactory results and the ultimate outcome, as determined by surgeons examining the patients in the Hospital clinic. Recent reports of the surgical treatment of varicose veins from other clinics have been reviewed.

The lack of proof that there is any one method which is superior to others in the treatment of varicose veins is demonstrated on our service by the simultaneous use of several operative procedures by surgeons on the three Services—men with the same relative ability and experience. During the past few years each of these three subdivisions of the Surgical Department has employed, almost exclusively, one of the three more common operative procedures—high saphenous ligation, multiple ligation, or stripping of the vein—without regard to the severity of the varicosities. It is believed that this nonselective factor adds considerably to the value of this study. The majority of retrograde injections of sclerosing solutions were done in the first two years of the period studied.

Patients complaining of varicose veins are first seen in our Varicose Vein Clinic, where the majority are treated by injections. The cases requiring more than this therapy are admitted to the hospital the day before operation. Almost without exception these patients have incompetence of the internal saphenous valves, as shown by a Brodie-Trendelenburg test, and 65 per cent were found to have incompetence of the communicating vessels as well. None gave evidence of obstruction of the deep veins by Perthe's test or modifications of this test.

The operations were carried out under local anesthesia by the resident staff, and consisted of five types of procedure. (1) High ligation of the internal

saphenous at its junction with the femoral vein, following a technic described in the earlier paper from this clinic,<sup>1</sup> care was exercised to divide all collaterals of the upper portion of the vein and to remove a segment of 4 to 6 cm, (2) high ligation of the saphenous vein at its junction with the femoral vein as in (1), plus multiple interruptions by ligation and division of the vein along its course, requiring three to seven incisions and averaging four, (3) high ligation of the vein as in (1), plus extirpation of a portion of the internal saphenous vein by means of the Mayo stripper. Two or three superficial incisions in the thigh were made along the course of the vein to secure and divide large collaterals and perforators, (4) high ligation as in (1), and retrograde injection of a sclerosing agent into the distal vein. In almost one-half of this group of cases the internal saphenous vein was also divided in the lower thigh and the distal segment injected. Five per cent sodium morrhuate was most often employed, usually injected by syringe through an urethral catheter as the catheter was withdrawn from the vein, (5) high ligation as in (1), and excision of a prominent varix in the lower thigh or calf.

Postoperatively, to occlude the remaining superficial venous circulation, the leg was immediately wrapped with three or four semielastic bandages applied while the foot is maintained in an elevated position, and reaching from groin to foot. The patients are ambulatory on the afternoon of the day of operation and, if possible, discharged from the hospital the next day. Sutures are removed in the Minor Surgery Clinic. Whenever indicated, the patients are referred to the Varicose Vein Clinic for the injection of sclerosing agents, and they are seen in the Follow-up Clinic at intervals of six and 12 months.

*Results*—Of the 365 consecutive cases reviewed, 288 were followed for at least one year, the average period being 18 months. Thus, we have followed 80 per cent of our cases long enough to show most of the poor results due to failure of the operative procedure. Moore and Knapp<sup>1</sup> indicated that beyond one year there is little change in the comparative results. We have repeated their method of determining this fact in Table VI and find no significant relative change in operative results as the follow-up period is lengthened (Table VI).

Of the 288 cases with adequate follow-up, 124 were treated unilaterally, while 164 required bilateral operations, making a total of 452 extremities which form the basis of this study. The percentage of bilateral involvement of 56, agrees with Steubner's<sup>2</sup> reported 52 per cent. The right extremity was affected in 51 per cent, the left in 49 per cent of the total. Ochsner,<sup>3</sup> McPheeters,<sup>4</sup> and Steubner<sup>2</sup> also failed to show predilection for either leg.

Females predominated, comprising 70 per cent of our series. This ratio of 3 to 1 is noted by McPheeters and by Bernstein,<sup>4</sup> Ochsner and Mahoney's series showed a larger proportion of women, but their cases included a large number of females in whom pregnancy and varicosities coexisted. In our series of cases 70 of the 200 women gave pregnancy as the inciting cause of the condition.

The average age of the patients was 46.5 years. Ochsner's nonpregnant patients averaged 48.4 years, McPheeters reported the highest incidence of varicose veins in the sixth decade.<sup>3, 4</sup>



The results of operation and postoperative sclerosing injections in our cases are classified in four groups (1) Excellent, which implies absence of symptoms and absence of significant varicosities, (b) good, which denotes marked improvement but with the presence of minor complaints or small varicosities, (3) improved, showing definite improvement but with symptoms and moderate varicose veins, and (4) poor, showing little or no improvement, development of ulcers or need of further operative treatment

Finally, because it is realized that any classification of results of treatment must be more or less arbitrary and subject to variables on the part of the patient and examining surgeon, the good and excellent results are combined as satisfactory and the improved and poor as unsatisfactory

In Table I the results are classified according to the operative procedure. Seventy-nine per cent of the whole series were found to have been satisfactorily treated with the best results obtained by multiple ligation, high ligation with retrograde injection, and stripping, in the order named (Table I)

TABLE I

Operative Procedure	No Cases	Results*					
		Unsatisfactory			Satisfactory		
		Poor %	Improved %	Total %	Good %	Excellent %	Total %
High ligation	103	7	24	31	36	33	69
Multiple ligation	121	5	7	12	48	40	88
High ligation and retrograde injection	103	7	8	15	42	43	85
Stripping	104	2	17	19	35	46	81
Ligation and excision	21	10	19	29	38	33	71
Total	452	21%			79%		

\* This shows percentages of satisfactory and unsatisfactory results obtained by the various procedures. Multiple ligation, high ligation with retrograde injection and stripping in the order named gave the best results while high ligation alone produced relatively unsatisfactory results.

Table II gives the average number of days of hospitalization required for each procedure. It is customary to discharge patients as soon as possible after operation because of the shortage of beds, and because it is felt that an early return to normal activity is a good prophylaxis against pulmonary embolism. Prolonged hospitalization, therefore, usually signifies the occurrence of complications, or the unwillingness of the patient to leave the hospital because of

TABLE II

Procedure	Average Days Hospitalization*
High ligation	3.6
Multiple ligation	3.8
High ligation and retrograde injection	4.4
Stripping	4.5
Ligation and excision	4.4

\* This shows the average hospitalization in days for each operation. It reveals that the more extensive procedures were followed by longer hospitalization.

## SURGERY OF VARICOSE VEINS

discomfort The table offers some information on the degree of pain suffered after the different procedures As might be expected, the simplest operations—high ligation and multiple interruption—were followed by a shorter stay in the hospital than were stripping and retrograde injection, both of which may produce painful extremities (Table II)

Table III presents the average number of postoperative sclerosing injections required to give satisfactory results following each operation (Table III)

TABLE III	
Operative Procedure	Average Number of Injections*
High ligation	4 3
Multiple ligation	3 4
High ligation and retrograde injection	2 0
Stripping	3 0
Ligation and excision	3 6

\* Average number of postoperative injections following each of the procedures Fewer injections were required after retrograde injection, stripping and multiple ligations

The postoperative complications—phlebitis, infection of the wound, and a questionable instance of pulmonary embolism—are presented in Table IV It will be seen that multiple ligation was followed by the largest number of complications, but, for the most part, these were minimal wound infections or failure of all incisions properly to heal at once One case required readmission

TABLE IV	
Operative Procedure	Complications*
High ligation	1 hemorrhage requiring reopening of the wound
Multiple ligation	6 superficial wound infections or delayed healing
High ligation and retrograde injection	1 severe bilateral phlebitis of internal saphenous
	1 superficial phlebitis
Stripping	1 hematoma of wound
	1 superficial phlebitis
	2 superficial wound infections
	1 questionable pulmonary embolism†

\* Complications following multiple ligation were more numerous than after other procedures but more severe after retrograde injection There were no fatalities

† Diagnosis not verified by examination

for three days, while the others were treated without difficulty in the Minor Surgery Clinic The most serious complication was a painful bilateral phlebitis of the internal saphenous system following retrograde injection of 5 per cent sodium morrhuate This patient required a total of 15 days' hospitalization

In contrast to the earlier report of cases from this hospital which included two deaths from massive pulmonary infarction following high ligation and excision, this series had no deaths An incident, suggestive of pulmonary embolism following a stripping operation, was reported to the clinic, but this diagnosis could not be confirmed by examination

## SUMMARY AND DISCUSSION

On the basis of the results obtained in the cases studied, it would seem that any operation which combines high ligation at the saphenofemoral junction with the addition of multiple interruptions of the saphenous vein, stripping of the vein, or retrograde injection of a sclerosing solution will give from 80 to 90 per cent satisfactory results.

The results of multiple ligation were slightly better than those following the other procedures but the higher incidence of wound infection and poor wound healing associated with it are undesirable. These complications of the operation probably are due to the fact that more incisions are required and that a larger area of the leg must be exposed at operation, hence, draping can be less precise. It is believed that greater care in technic might eliminate this factor.

Table III, giving the number of postoperative injections following each procedure, indicates that to sclerose isolated segments resulting from multiple interruptions, necessitates a larger number of postoperative injections than are needed after operations which remove the vein by stripping or obliterate it by injection at the time of operation. However, since multiple ligation is a simple procedure it should not carry the same risk of embolism which radical extirpation of the vein or the injection of sclerosing solutions do.

Extirpation of the saphenous vein with the Mayo stripper gave good results in a high percentage of cases. Since, in this procedure, the vein actually is removed and all communicators severed, these satisfactory results can be expected. That they were not better than those following other operations may be due to the fact that the vein generally was stripped to just below the knee and incompetent communicators with the external saphenous or the deep veins of the calf were not adequately treated. If the operation is used, the stripping probably should be continued down to the ankle, as recently described by Hodge,<sup>6</sup> or combined with multiple ligations in the calf. Ochsner and Mahorner, in their monograph,<sup>4</sup> expressed fear of a high incidence of pulmonary infarction following any attempt at extirpation—a reasonable consideration not borne out by experience. The only case with symptoms suggestive of embolism, however, followed this procedure. Stripping the saphenous vein under local anesthesia usually causes the patient great discomfort and general anesthesia prevents their early mobilization.

High ligation with retrograde injection also was effective, and following this procedure, the smallest number of postoperative injections were required to obtain satisfactory results. This operation has been recommended by many experienced surgeons and has gained wide acceptance. Ochsner and Mahorner<sup>4</sup> consider it the procedure of choice when combined with low ligation in cases with incompetent communicators. From the experience with 2,582 ligations of varicose veins, McPheeters<sup>5</sup> concludes that the operation gives uniformly good results. In 1942, a series of reports from the Mayo Clinic, by Waugh and Heyerdale, and associates,<sup>7, 8</sup> recommend it as the procedure of choice. Pratt<sup>9</sup> reports 90 per cent and Sears<sup>10</sup> 81 per cent satisfactory results following this

operation Lyall<sup>11</sup> describes the use of high ligation with retrograde injection in 200 private patients and Pearce<sup>12</sup> reported a series from an Army hospital treated with good results

Retrograde injection however, has the disadvantage of the danger of producing painful and serious reactions In 1942, Vaughn<sup>13</sup> found 44 cases of fatal pulmonary embolism following the injection therapy reported in the literature and added one of his own Atlas,<sup>14</sup> in 1943, called attention to the hazards of injecting sclerosing solutions either directly or retrograde, and expressed the opinion that injection at the time of operation was contraindicated

TABLE V

Operative Procedure	Incompetent Communicators		Competent Communicators	
	Results		Results	
	Unsatisfactory	Satisfactory	Unsatisfactory	Satisfactory
High ligation*	18	44	10	27
	62		37	
Multiple ligation	7	74	4	33
	81		37	
Stripping	14	50	5	30
	64		35	
Ligation and retrograde injection	8	50	4	38
	58		42	
Ligation and excision	1	11	3	5
	12		8	
Total	277		159	

\* Classification of results obtained with each procedure is related to the preoperative condition of the communicators, it shows the inadequate results achieved after high ligation in cases even without demonstrable incompetent communicators

cated In our series the operation was followed by serious complications in a few cases and, quite generally, by prolonged hospitalization In recent years the method has been largely abandoned at the New York Hospital—not because of a great number of serious complications but because of the postoperative discomfort associated with the operation and because the results were not so satisfactory as following other procedures

In our experience, simple high ligation has been relatively unsatisfactory Only 69 per cent of the patients treated in this manner could be said to have satisfactory results A higher percentage of good results could hardly be expected from a method which gives no consideration to the communicating vessels With the added procedure of postoperative injections, the results might be expected to be adequate for an extremity in which no incompetence of the communicating vessels could be demonstrated Our results offer evidence against this assumption In Table V are presented the results according to the operation and the preoperative condition of the communicating vessels when this information was available (436 of 455 extremities) It will be seen

TABLE VI  
PERIOD OF FOLLOW UP

Operative Procedure†	1 year			1 5 years			2 years			2 5 years			3 years			3 5 years			4 years			5 years			6 years		
	P*	I*	G* E*	P	I	G	E	P	I	G	E	P	I	G	E	P	I	G	E	P	I	G	E	P	I	G	E
High ligation	6	13	17	19	0	7	10	7	1	1	4	3	0	3	3	2	0	1	0	0	0	0	0	0	0	0	0
	(55)				(24)			(9)			(8)		(1)			(2)			(2)			(3)			(2)		
Multiple ligation	0	2	23	13	0	1	18	18	2	1	4	9	0	2	6	9	1	0	1	4	4	1	5	1	0	0	0
	(38)				(37)			(16)			(17)		(6)			(11)			(2)			(0)			(0)		
Stripping	0	5	13	20	0	3	5	9	2	2	8	12	0	1	1	5	0	3	1	0	0	0	1	1	0	0	0
	(38)				(17)			(7)			(24)		(4)			(2)			(0)			(6)			(0)		
Ligation and retrograde injection	0	1	11	17	6	2	14	7	5	2	12	7	1	0	6	1	0	3	2	5	0	0	0	4	0	0	0
	(29)				(23)			(26)			(8)		(10)			(4)			(0)			(0)			(0)		
Ligation and excision	0	1	4	4	0	0	2	2	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	(9)				(4)			(3)			(0)		(0)			(1)			(1)			(0)			(0)		

\* P—poor, I—improved, G—good, E—excellent

† Cases treated by each operation arranged according to result and length of follow up, to show that there is no change in the comparative results of the operations as the follow up period is lengthened

that 10 of the 37 cases (27 per cent) without demonstrable incompetence of communicators, treated by high ligation, gave unsatisfactory results, while only four of the seven (11 per cent) treated by multiple ligation, five of 35 (14 per cent) subjected to stripping, and four of 38 (10 per cent) treated by ligation and retrograde injection were unsatisfactory. Further evidence can be deduced from the results in cases with proven incompetent communicators subjected to high ligation (29 per cent unsatisfactory), which were only slightly worse than those without such incompetence (27 per cent). Finally, high ligation with only one interruption—by excision of a varix in the thigh or calf—gives more satisfactory results than high ligation alone. It is believed that even when no incompetent communicators can be demonstrated at the time of operation, interruption of the saphenous at, or below, the usual site of the communicators should be carried out on the assumption that incompetence was not detected by the clinical tests or that the communicating vessels may become incompetent later. Any communication with an incompetent external saphenous vein should be given careful consideration, as has been emphasized by Heyerdale.<sup>15</sup>

## CONCLUSIONS

(1) High ligation of the saphenous vein combined with multiple ligations, retrograde injection or stripping of the vein have been

found to give between 80 and 90 per cent satisfactory results in 452 cases of varicose veins observed for one year or more after operation

(2) Hospitalization was longest and degree of discomfort to the patient was greatest following retrograde injection or stripping, and least after high ligation or multiple ligations

(3) Complications were more frequent after multiple ligation though the majority were not serious, and phlebitis occurred more often after retrograde injection. There were no proven cases of pulmonary embolism, and no deaths

(4) Simple ligation with retrograde injection required the smallest number of postoperative sclerosing injections to attain satisfactory results

(5) Multiple ligation, combining the advantages of a safe procedure easily performed under local anesthesia, with superior results is in our experience, the operation of choice

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# PERSISTENT OMPHALOMESENTERIC (VITELLINE) ARTERY CAUSING INTESTINAL OBSTRUCTION AND GANGRENE OF MECKEL'S DIVERTICULUM\*

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AMONG THE RARER CONDITIONS which are encountered in surgery those which precipitate practical problems are especially worthy of consideration. Persistent omphalomesenteric, or vitelline, artery falls into this category. Its presence is one of the infrequent causes of intestinal obstruction. The literature contains only 16 cases in which a persistent omphalomesenteric artery caused symptoms, and, of this number, evidence of intestinal obstruction was found at operation or autopsy in 11 cases (69 per cent). In addition, six asymptomatic cases have been reported, making a total of 22 cases of persistent omphalomesenteric artery in the literature.

Of these 22 cases, a Meckel's diverticulum of the ileum was present in 13 (59 per cent). Of the 11 cases presenting evidence of intestinal obstruction at operation or autopsy, 10 (91 per cent) had a coexistent Meckel's diverticulum. This association is not surprising if we consider the origins and fates of these structures in the embryo.

## EMBRYOLOGY<sup>1 2 4 13 18 25 26</sup>

The yolk sac is demonstrable at the second week of intra-uterine life. The yolk sac and the primitive gut are connected to each other by the yolk-stalk, or vitelline (omphalomesenteric) duct. The part of the gut to which the omphalomesenteric duct is attached is the midgut, from it are derived the small intestine (except the first part of the duodenum), the cecum, the ascending colon and the transverse colon.

During the first weeks of embryonal development, the aorta is a paired structure (Fig. 1). From each portion a prominent vessel courses ventrally to the primitive gut and thence out along the yolk-stalk to reach the yolk sac. With the merging of the paired aorta into a single aorta the two main ventral branches merge and the resultant vessel comes to be the superior mesenteric artery (Figs. 2 and 3), or it may be postulated that in certain cases these ventral branches do not merge and that one of the large ventral branches grows while the other recedes, the developing one becoming the superior mesenteric artery. If the other ventral branch does not recede completely but persists in an attenuated form it may be identified later as the persistent omphalomesenteric vessel (Fig. 4), at least that part running from the ileal mesentery to a Meckel's diverticulum or to the under surface of the umbilicus, or to both. However, this theory of formation may not be complete. Where the main ventral vessels have merged to one main trunk this single ventral

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artery reaches the forming midgut and the artery's continuation out along the vitelline duct is a paired one. At the time when the vitelline duct separates from the midgut (after six weeks) the yolk sac and the duct disappear. At this time one, or more, of the vessels which ran along the vitelline duct from gut to yolk-sac may not disappear but persist and be labeled a persistent vitelline artery.

If the gut-end of the omphalomesenteric duct persists and remains in communication with the bowel it is designated a Meckel's diverticulum. This is found at 2 to 3 per cent of autopsies.

Persistence of the omphalomesenteric artery manifests itself as an adventitious intra-abdominal, fibrous band (which may, or may not, contain a patulous vessel) covered by peritoneum. The persistent artery in all but a few cases, is attached at each end (13 cases out of 22 reported, or 59 per cent). Usually one end is attached to the anterior abdominal wall and the other end is attached either to the ileal mesentery or to a Meckel's diverticulum. Less often, (seven cases, or 32 per cent) it connects a Meckel's diverticulum to the ileal mesentery. In a few cases the cord is attached at only one end. In these latter instances, both in infants the unattached end hung harmlessly free in the abdomen, and gave no symptoms.

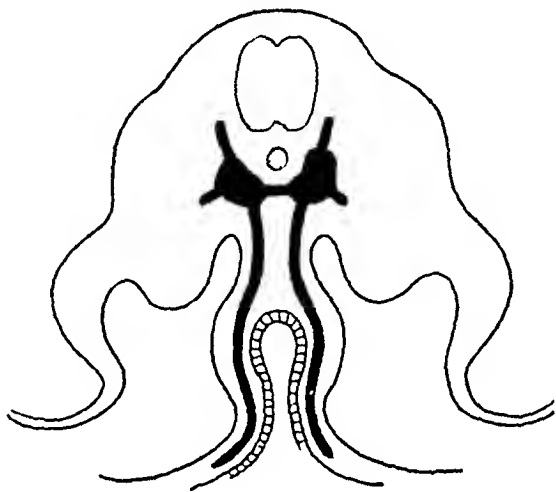


FIG 1—Cross-section of a human embryo at approximately two and one-half weeks. This shows paired aortae joining to become a single vessel. The two main ventral branches are shown going down to the forming midgut.

#### LITERATURE AND CLINICAL CONSIDERATIONS (TABLE I)

The first cases on record were two reported by Sandifort,<sup>20</sup> in 1777. Meckel,<sup>16</sup> in 1809, reported a case, and was the first writer to suspect the true origin of this condition. Fitz,<sup>8</sup> in 1884, gave an excellent résumé of the cases reported up to that date, disproved the view that these fibrous bands were inflammatory in origin, and clearly described the manner in which they arose. Contemporary reports are those of Postoloff,<sup>17</sup> and of Smithy and Chamberlin,<sup>24</sup> in 1946.

The first symptomatic cases in the literature varied in age from four months to "old age." The youngest case of intestinal obstruction was one year old.<sup>23</sup> Of the six asymptomatic cases, only one was an adult.<sup>5</sup>

Three clinical pictures may be seen:

(1) *Acute Intestinal Obstruction*, with evidence of same at operation or autopsy. Eleven cases (69 per cent) were in this group.<sup>6, 7, 8, 14, 15, 17, 20, 23</sup> Survival of such a case has not been reported.



(2) *Recurrent Abdominal Pain*, occurring over periods of several months to many years. Four cases (25 per cent) were in this group<sup>3, 10, 22, 24</sup>. Pain was in the right lower quadrant, epigastrium or periumbilical area. Excision of the band resulted in cure in all cases.

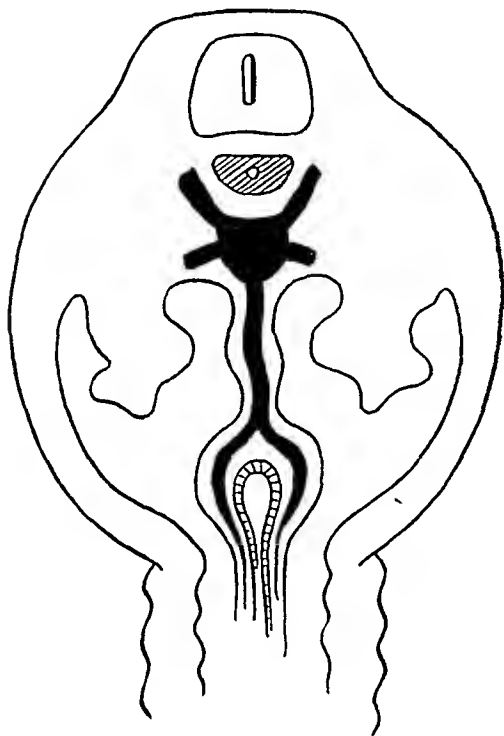


FIG 2—Cross-section of embryo at about five weeks. There is a single aorta and one main ventral branch, the other having merged, or regressed. The midgut is almost closed and the connection between it and the yolk-sac beyond is now a narrow tube. On each side of it branches of the principle ventral artery (especially the two main trunks) continue to the wall of the yolk sac. The midgut will close and the connection between it and the yolk-sac will regress.

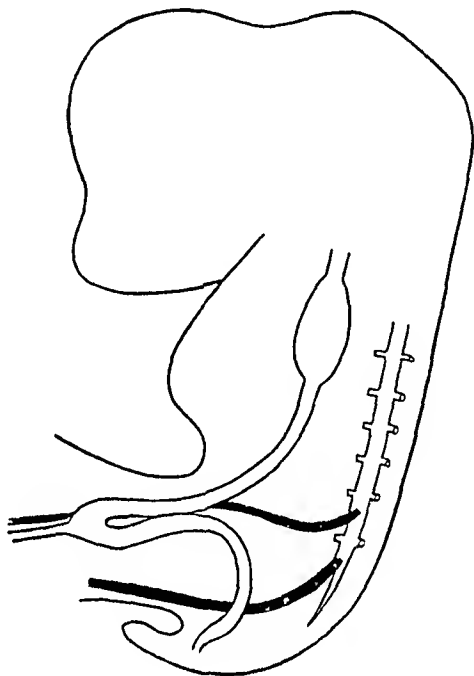


FIG 3—Sagittal section of embryo at about five and one-half weeks. The main ventral artery is seen coming from the aorta to the almost closed midgut. One branch of it is shown continuing along with the still-present vitelline duct. Shown below is one of the umbilical arteries arising further down the aorta and making its exit into what is to be the umbilical cord.

(3) *Intra-abdominal Hemorrhage*. Only one such case has been reported.<sup>9</sup> In a four-month-old infant, cauterization of granulation tissue at the umbilicus necessitated traction on the pedicle by which it was attached. Death resulted from intra-abdominal hemorrhage. Autopsy revealed a cord extending from the umbilicus to the ileal mesentery, the cord was attached to a branch of the superior mesenteric artery. Another nearby branch of the superior mesenteric artery had ruptured.

**Case Report**—No 9555. E. M., male, white, age three years, was admitted to the Nazareth Hospital, on June 22, 1946. The patient's mother stated that the child had suffered periumbilical pain and vomiting for three days. No symptoms referable to

# OMPHALOMESENTERIC ARTERY

TABLE I

## COLLECTED CASES OF PERSISTENT VITELLINE ARTERY

Author	Date	Sex	Age	Findings
Standiford <sup>20</sup> Case 1	1777	?	Adult	Sacciform diverticulum, with blind extremity attached by tough cord to left side of cecum, forming noose to constrict intestine Fatal intestinal strangulation
Case 2	1777	?	?	Diverticulum of ileum adherent at tip to mesentery Through ring thus formed intestine had become strangulated
Case 3	1793	?	Infant	'Appendix arising from ileum, united at its end to upper part of mesentery by narrow strong thread Asymptomatic
Eschricht <sup>6</sup>	1834	F	"Old	Meckel's diverticulum attached by persistent vitelline artery to ileal mesentery, forming loop which caused fatal strangulation of intestine
Falk <sup>7</sup>	1835	?	20 yrs	Persistent vitelline artery uniting free end of Meckel's diverticulum with ileal mesentery to form loop Fatal intestinal strangulation
King <sup>14</sup> Case 1	1843	?	14 mos	Patent Meckel's diverticulum adherent to umbilicus forming enteric fistula Adventitious cord connecting diverticulum to ileal mesentery compressed the ileum, causing fatal intestinal obstruction
Case 2	1843	?	?	Cord extending from base of Meckel's diverticulum to ileal mesentery causing fatal intestinal obstruction
Mahomed <sup>14</sup>	1875	M	18 yrs	Band extending from anterior abdominal wall midway between pubis and umbilicus, to ileal mesentery, acted as noose to cause fatal intestinal obstruction Meckel's diverticulum present
Fritz <sup>8</sup> Case 1	1884	?	28 yrs	(Warren Museum Specimen No 496, Improvement Collection) Diverticulum of ileum with cord proceeding from end of diverticulum to upper surface of mesentery Through ring thus formed intestines became strangulated with fatal results
Case 2	1884	M	21 yrs	Diverticulum of ileum with tendinous cord proceeding from diverticular mesentery to umbilicus Fatal intestinal strangulation
Shcen <sup>23</sup>	1916	M	1 yr.	E T L Umbilicus polypus excised and base cauterized Death one week later of intestinal strangulation Meckel's diverticulum attached to umbilicus by cord Ileum herniated through hole in diverticular mesentery, strength of constricting cord of mesentery largely due to vessel transversing it
Postoloff <sup>17</sup>	1946	M	38 yrs	Attacks of cramping abdominal pain for two years Cord extending from umbilicus to ileal mesentery causing fatal intestinal strangulation No diverticulum
Fraser and McCartney <sup>9</sup>	1920	?	4 mos	Granulation tissue attached to pedicle in umbilicus Actual cauterization performed, necessitating traction of pedicle, which caused rupture of branch of superior mesenteric artery in ileal mesentery with fatal intra-abdominal hemorrhage Cord extending from umbilicus to ileal mesentery cord was attached to branch of superior mesenteric artery No diverticulum
Shaw <sup>22</sup>	1925	F	43 yrs	Right lower quadrant abdominal pain since childhood Hysterectomy performed for vaginal bleeding, at operation found band extending from ileal mesentery to anterior abdominal wall near right inguinal ring Band transfixed omentum No diverticulum Cure followed excision of band

TABLE I *Continued*

## COLLECTED CASES OF PERSISTENT VITELLINE ARTERY (Continued)

Author	Date	Sex	Age	Findings
Grueter <sup>10</sup>	1931	M	21 yrs	Repeated attacks right lower abdominal pain Persistent omphalomesenteric artery extended from umbilicus to ileal mesentery No diverticulum Excision of band resulted in cure
Buchanan and Wapshaw <sup>7</sup>	1940	?	12 yrs	Intermittent colicky pain in right lower quadrant and per-umbilical area with vomiting Persistent vitelline artery extended from umbilicus to ileal mesentery No diverticulum No obstruction at operation Excision of band resulted in cure
Smithy and Chamberlain <sup>24</sup>	1946	M	25 yrs	Intermittent epigastric and perumbilical pain with vomiting for six months Relieved by reclining Fibrous cord extending from umbilicus to ilcal mesentery Cord looped over ileum to left of latter so as to support weight of terminal ileum and cecum when patient was erect No diverticulum No obstruction at time of operation Excision of cord resulted in cure
Derbes and Hoge <sup>5</sup>	1937	?	Adult	Asymptomatic Dissecting room cadaver—death from tuberculosis From free end of Meckel's diverticulum cord extended to umbilicus Patent omphalomesenteric vessels run along mesenteric border of diverticulum At top of diverticulum these were joined by branches from inferior epigastric vessels From this anastomosis runs impervious arterial connection to right obliterated hypogastric artery Two nonpatent vessels run inferiorly to fascia surrounding urachus on visceral end omphalomesenteric vessels join ileal of superior mesenteric vessels
Meckel <sup>16</sup>	1809	?	Infant	Asymptomatic Vessel unattached at one end
Ruge <sup>19</sup>	1877	?	Infant	Asymptomatic Vessel unattached at one end
Gesell <sup>11</sup>	1938	?	New born	Asymptomatic Death from intracranial hemorrhage Cord attached to umbilicus and to mesentery
Hyrtl <sup>1</sup>	1870	?	?	Asymptomatic 'Very fine thread—running from mesentery to side of peritoneum where umbilical artery was lacking

the urinary tract were offered. There was no constipation nor diarrhea. Past medical history was essentially negative. The parents were in good health, one sibling was living and well.

Physical examination revealed a sturdy white male child showing obvious restlessness. Temp 98.6° (R). Pulse 96. Respirations 22. There was moderate tenderness on deep palpation in the right lower quadrant of the abdomen. No distention, rigidity nor rebound tenderness were elicited. Peristaltic sounds were normal. Digital rectal examination was negative. *Laboratory Data*: R B C 3,150,000, Hb 71 per cent, W B C 12,500, neut 90 per cent, lymph 10 per cent. Urinalysis Neg.

Because of increasing restlessness, diagnostic spinal tap was performed six hours after admission, the findings were normal.

Twelve hours after admission, his temperature rose to 101.4° (R), pulse to 128, and respirations to 38. Examination then revealed abdominal distention, generalized rigidity and tenderness, most marked in the right lower quadrant. Peristaltic sounds could not be heard. The patient was prepared for surgery, and given 500 cc of 5 per cent glucose in saline intravenously.

*Operation*—Under nitrous oxide-ether anesthesia a right pararectus incision was made (Fig 5). On opening the peritoneum, there was seen a gangrenous, swollen Meckel's diverticulum of the ileum, the diverticulum was 7 cm in length. There was also apparent a tough, rounded, taut adventitious cord, 3 cm in diameter, proceeding from the umbilical area posteriorly and towards the right for a distance of 3 cm to attach to the mesentery of the diverticulum thence, after leaving the mesentery of Meckel's diverticulum, it proceeded for another 3 cm to end in the base of the ileal mesentery.

The diverticulum itself was completely black, and there was torsion of its neck. It was presumed that the sac had looped itself through the opening between itself and the proximal portion of the persistent vitelline artery (that running from its own mesentery to the base of the ileal mesentery). A loop of ileum had slipped through the noose formed by the latter part of the cord and had become obstructed. The serosa of the obstructed bowel was injected but viable. The intestine proximal to the obstructed loop was distended, that distal to the loop was collapsed. The vessel-containing cord was clamped, ligated and divided in four places, and removed in two sections. The Meckel's diverticulum was untwisted and resected. The abdomen was closed without drainage.

*Postoperative Course* Four days postoperatively, the temperature suddenly rose from normal to 103.6 (R). The patient was restless, the abdomen distended and tympanic. Penicillin 200,000 units i-m given every three hours. On the following day, the temperature dropped to normal and remained so, the abdominal distention was relieved. The patient was discharged in good condition on the 11th postoperative day. Seen six months following discharge, the patient was found to be in excellent condition, and without symptoms.

*Pathologic Report* "(A & B) Club-shaped, sac-like piece of tissue, 7.2 cm in length. Blind end is larger, and measured 2.8 cm in diameter, the other end measured 1.9 cm in diameter. Wall is thickened and covered with fibrin, and is dark purplish-red. On one side is a small vessel coursing along its middle, 3 cm in length. Each end has a small catgut ligature, and is 2 to 3 mm in diameter.

"(C) Wall, necrotic and purplish-red, and measures 3 to 4 mm.

"(D) Rounded, reddish-brown structure, 2.9 cm long and 3 mm in diameter, filled with coagulated blood. Catgut ligature on each end.

"Microscopic (D) Zone of connective tissue, infiltrated with neutrophils. Numerous hyperemic capillaries are noted."

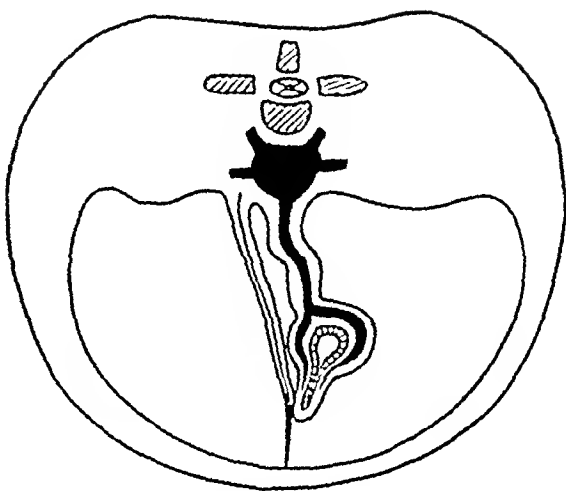


FIG. 4—Schematic drawing of cross-section of embryo at about six and one-half weeks showing gut incompletely closed, a small pouch persisting where the vitelline duct led off. This is a Meckel's diverticulum. Along the side of the mesentery of the intestine the remains of one of the main ventral vessels runs out to the diverticulum and, thence, to the under surface of the abdominal wall. This is the persistent vitelline artery.

## SUMMARY

1. The embryology of the omphalomesenteric artery is presented. Persistent omphalomesenteric artery is explained on the basis of the failure of the primitive-paired main ventral arteries to fuse, one continues to develop

and becomes the superior mesentery artery, the other persists in an attenuated form. This theory would explain, most logically, those cases in which the residual artery extends from the mesentery of the ileum to a Meckel's diverticulum (and continues in some cases to the under surface of the umbilicus) or extends directly from the mesentery to the under surface of the umbilicus. This type truly deserves the name omphalomesenteric artery.

Persistence of one of the vessels which run along the vitelline duct, and which could have been a continuation of one of the pair of main ventral vessels or a continuation of the single fused main ventral vessel, would explain

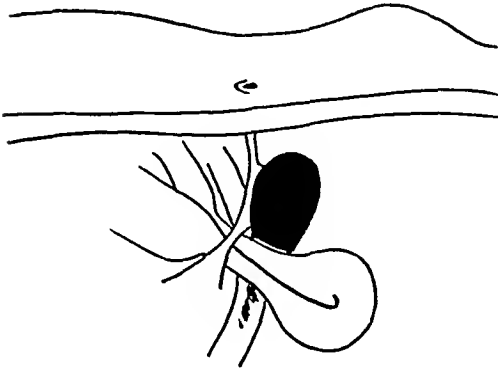


FIG 5—Illustrated are the conditions found at operation in the present case. The persistent remains of the vitelline artery, with its coverings, extends from the under surface of the umbilicus to the gangrenous Meckel's diverticulum, and, thence, to the mesentery of the ileum. Looping through the noose formed by this proximal portion is the segment of small bowel, which was incarcerated.

those cases which clinically present a persistent vessel or the remains thereof, running from the ileum or from a Meckel's diverticulum to the under surface of the umbilicus. Such a vessel seems better designated as a persistent vitelline artery.

2 The literature of persistent omphalomesenteric arteries is reviewed, and the clinical significance of this condition is discussed.

3 A case of intestinal obstruction due to persistent omphalomesenteric artery is presented. The presentation of this case is of interest for the following reasons:

(a) The rarity of persistent omphalomesenteric artery.

(b) Survival has never previously been reported in such a case showing

evidence of intestinal obstruction at operation.

(c) Gangrene of Meckel's diverticulum as a result of torsion of its neck contributed to, and maintained by, a taut persistent omphalomesenteric artery has not previously been described.

4 No characteristic set of signs and symptoms can be called pathognomonic of persistent vitelline artery. The symptoms vary with the complication produced. The important thing is to recognize the presence of an "acute" abdomen, and the diagnosis of the persistent vitelline artery is really only possible with the abdomen open. It is well to know, however, that it may be one of the underlying causes of intra-abdominal pathology, and that one may occasionally encounter it.

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# HOW LONG SHOULD AN EXTREMITY BE IMMOBILIZED AFTER NERVE SUTURE<sup>3,4</sup>

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END-TO-END SUTURE of a nerve is hardly ever possible without the use of various procedures for overcoming gaps which result from the loss of substance of nerves or the retraction of their stumps. The methods commonly used for gaining length consist of the often extensive freeing of the nerve, rerouting or suturing it with the neighboring joints flexed. Even when these steps are taken it is sometimes necessary to introduce nerve grafts, but end-to-end suture is preferable to the use of grafts provided that this can be accomplished without great strain on the suture line. In those instances where joints must be flexed in order to bring nerve ends into apposition and remove tension from the suture line, the question arises as to how long the limb must be immobilized in the flexed position. There exists a considerable degree of difference with respect to practice in such cases. Groff and Houtz<sup>1</sup> have suggested a two-week period as adequate while Hambly<sup>2</sup> advocates immobilization of the extremity for a period of 9-12 weeks following nerve repair. The surprisingly high incidence of separation at the suture site of 75 per cent (44 out of a total of 604 nerve sutures) reported by Whitcomb<sup>3</sup> was probably to a large extent attributable to inadequate immobilization of the sutured nerve since in some cases "fairly rapid extension of the flexed joint as early as two weeks after operation" was carried out. It is apparent that the period of immobilization must be long enough to avoid rupture of the suture site when the joint is extended. On the other hand, one must avoid too prolonged fixation of the joint since the inevitable muscle atrophy and periarthicular changes that ensue delay or even prevent recovery of function. Active and passive motion of the joint over which the sutured nerve passes must not be started before satisfactory healing of the suture line has occurred but it must not be delayed unnecessarily beyond this point. An attempt has been made in this study to resolve this apparent dilemma by the performance of a series of experiments upon rabbits and dogs. Microscopic studies of the process of healing at the suture line together with determinations of the tensile strength of the sutured nerve were made.

A previous attempt was made to settle this problem by Miller<sup>4</sup>. He carried

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\* This work was done under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and the Jewish Hospital of Brooklyn.



FIG 1—(A) Nerve sutured with plasma clot and removed four days after operation. Union of stumps has not occurred (Hematoxylin and eosin,  $\times 22$ )  
(B) Five-day-old sutured nerve. Streaming of cells across the suture site has occurred (Hematoxylin and eosin,  $\times 32$ )  
(C) Nerve sutured with plasma clot seven days before excision of specimen. Slight seepage of plasma into suture line has occurred and there has been cellular proliferation between the stumps (Hematoxylin and eosin,  $\times 20$ )



out experiments in 11 dogs, suturing the sciatic nerve with silk or catgut. Tensile strength determinations were made of the suture site at the following intervals after operation: 1 week, in 3 dogs; 2 weeks, in 2; 3 weeks, in 2; 4 weeks, in 1; and 5 weeks, in 3 animals. Miller concluded that the strength of the suture line was "practically as great at the end of the third week as at the end of the fourth or fifth week." Comparisons of the strength of the suture line with the strength of the intact nerve were not made. Singer<sup>5</sup> showed that the tensile strength of the sciatic nerve of rabbits in which suture was accomplished by the use of fibrin film and thrombin, remained approximately constant during the first three postoperative days, but dropped by the fourth day to an average of 90 Gm. from an initial value of just over 100 Gm. After the fourth day it rose to an average of 338 Gm. on the sixth day and 625 Gm. on the tenth day. The results showed that "sufficient healing occurred by the end of the fifth or sixth day to ensure retention of the stumps without the aid of the suture material." Singer's studies were not carried beyond ten days after suture.

#### METHOD

In our experiments both sciatic nerves in a series of 14 rabbits were exposed, severed and then sutured by the use of the autologous plasma clot technic.<sup>6</sup> Two of the three untwisted strands of No. 00 corticelli black silk were used as tension sutures to approximate the nerve ends and accurate apposition was achieved with the aid of plasma clot. The tension sutures were employed in order to avoid strain on the suture site during the unrestricted movements of the animal following recovery from the anesthetic. The animals were sacrificed at various intervals after operation, and 4-cm. segments of the nerve were removed (2 cm. to each side of the suture site). Also, 4-cm. segments of intact sciatic nerve were excised. The silk tension sutures were removed and tensile strength measurements were made of the suture site, the intact nerve, and of one of the withdrawn silk tension sutures from each nerve. For the purpose of microscopic study, the same technic of nerve suture was used upon the sciatic nerves of dogs, with the exception that tantalum wire (.003-inch in diameter), which causes less tissue reaction than silk,<sup>6</sup> was used as tension sutures. Observations were made upon several hundred such nerves at intervals ranging up to 18 months after operation. This material was prepared for study by a variety of histologic technics (hematoxylin and eosin, Laidlaw's connective tissue method, Gros-Bielschowski technic for axis cylinders, and osmic acid technic for myelin sheaths). The results of this study of nerve regeneration will be published later. For our present purpose, the observations upon this material concern the process of healing at the suture line with reference to restoration of its structural continuity.

The technic employed for the measurement of tensile strength was essentially that described previously.<sup>7</sup> Increasing increments of weights were applied until rupture of the nerve took place.

OBSERVATIONS

Few monocytes and polymorphonuclear leukocytes appear within the plasma cuff as early as 24 to 48 hours after nerve suture, and an occasional fibroblast may be seen at this time. The fibroblasts increase in number and a

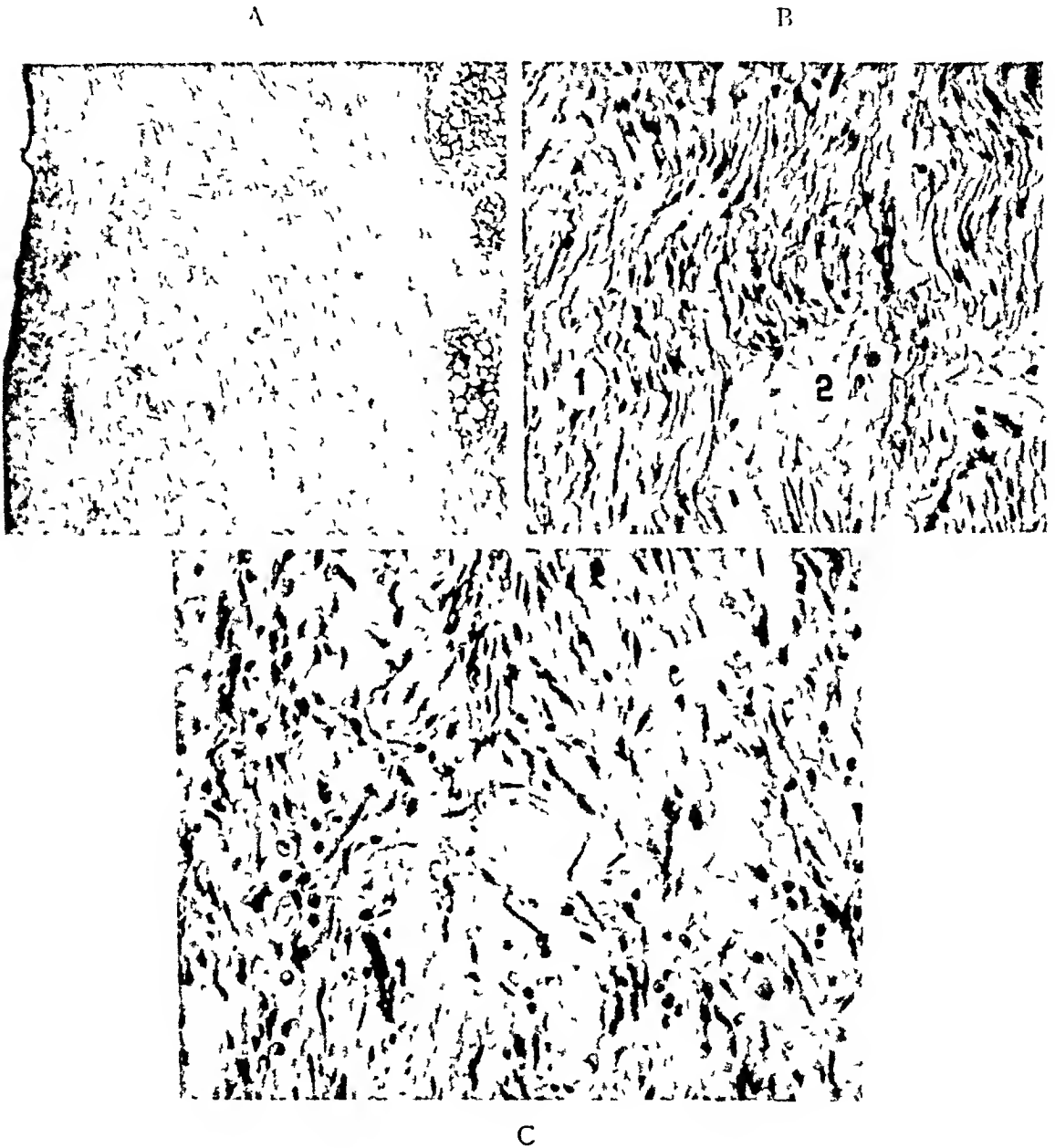
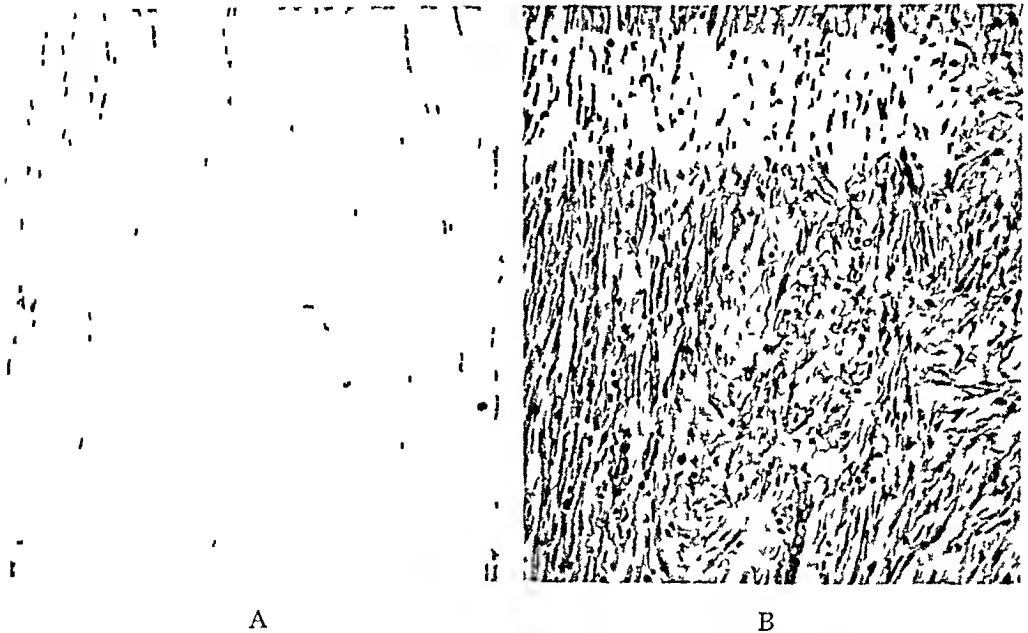


FIG 2—(A) Nerve sutured with plasma clot and removed nine days later. Incomplete union of the stumps has occurred. This is more apparent in (B) and (C) where macrophages as well as proliferating cells of the fibroblastic and schwannian types are seen. Cellular and fibrous continuity is seen in (B) at 1, but not at 2. Microphotographs taken from sections stained with hematoxylin and eosin, (A)  $\times 20$ , (B)  $\times 200$ , (C)  $\times 200$ .

normal epineurium is reconstructed from the plasma sheath in seven to ten days. Within a period of two to three days after suture mild, degenerative, exudative and proliferative changes appear at the junction of the nerve stumps

Few polymorphonuclear leukocytes together with some monocytes and lipophages appear at this time. These latter cell types may persist for several weeks. Fibroblasts and Schwann cells proliferate and may frequently be seen streaming out into a slight exudate between the nerve stumps. Although Schwann cells are usually larger and present more oval nuclei than fibroblasts the differentiation between these cells may be impossible without the aid of special staining technics.<sup>8</sup>

As early as 3 to 5 days after suture, cells may be seen streaming across the suture line (Fig 1B), but occasionally signs of such cellular proliferation are



A

B

FIG 3—(A) Nerve sutured with plasma clot and removed 11 days later. Almost complete cellular and fibroblastic continuity has occurred (Laidlaw's lithium silver carbonate impregnation for connective tissue,  $\times 20$ ).

(B) High power view of nerve seen in (A). Structural continuity of framework of nerve is seen on the left but not on the right, where the cellular orientation is less satisfactory (Hematoxylin and eosin,  $\times 150$ ).

strikingly absent (Fig 1A). Sections taken nine days after operation have shown structural continuity of schwannian and endoneurial sheaths, although not uniformly in all cases (Fig 2). In some nerves at this age, structural continuity was seen at one portion of the suture line, whereas examination of adjacent areas revealed the presence of a coagulum occupied by monocytes and lymphocytes. This same variation in appearance of the suture line was seen in specimens examined 11 days (Fig 3), and to a less extent 14 days after suture (Figs 4 and 5). In some instances suture lines nine, 11 and 14 days old proved to be remarkably free from cellular infiltration (Fig 5B). In practically all cases of sutures 18 days or particularly three or more weeks old, complete restoration of structural continuity has occurred (Figs 6 and 7).

The growth of nerve fibers through the suture line may be demonstrated at this age

At times as a result of seepage of plasma into the nerve junction, or because of faulty apposition of nerve ends, Schwann cells, fibroblasts and connective tissue fibers become oriented transversely to the plane of the nerve. Although this is an undesirable occurrence because of the ensuing disorientation of nerve fibers at the suture line, the intrusion of a few drops of plasma at the suture line has been found to be compatible with satisfactory regeneration.

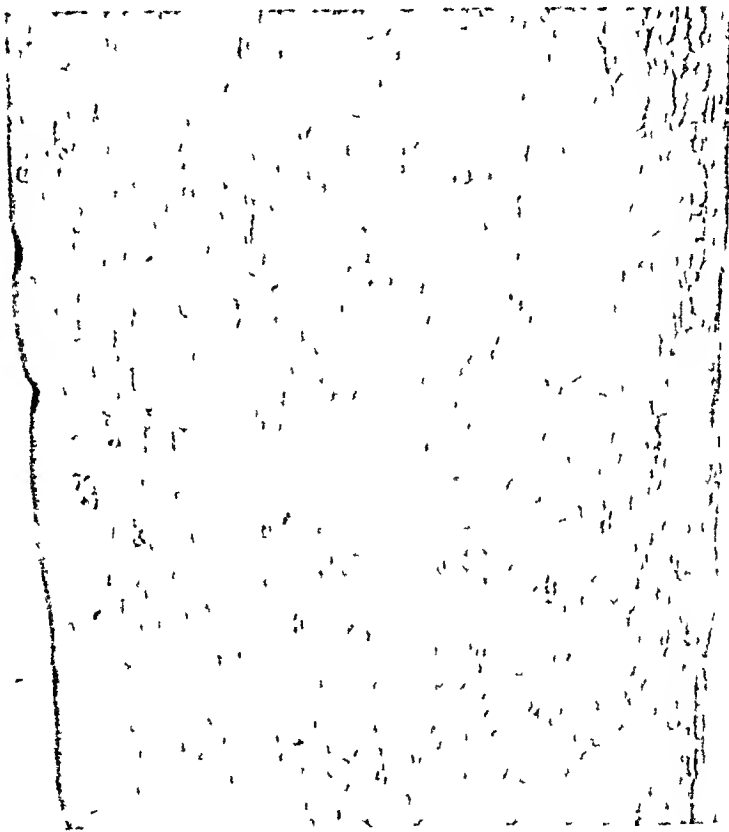
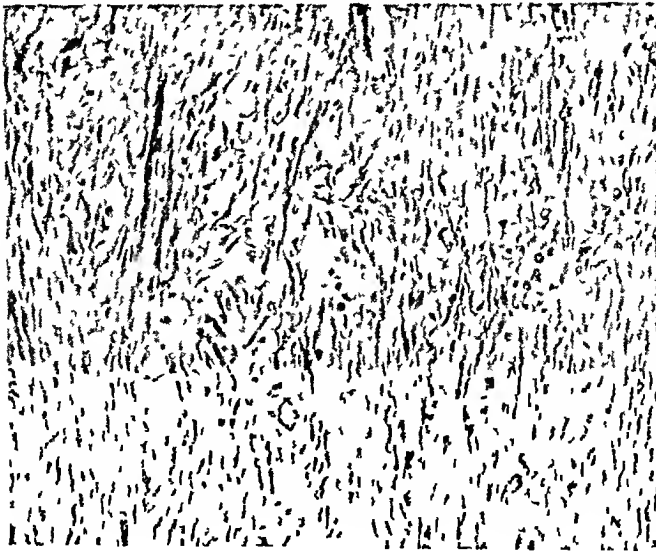
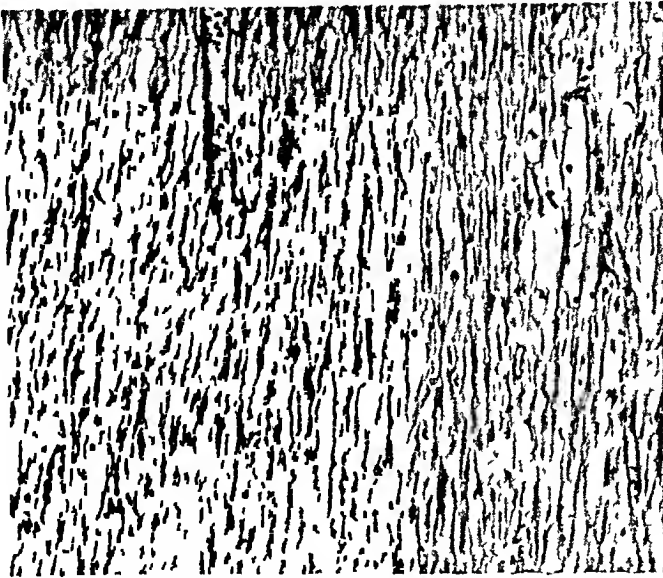


FIG. 4—Nerve sutured with plasma clot and removed 14 days later. Restoration of continuity has occurred (Hematoxylin and eosin,  $\times 32$ ).

Examination of Table I tends to confirm the histologic observations, in that the suture site regained, or even exceeded, the strength of the intact sciatic nerve 19, or more, days after operation. It is of interest that in rabbits Nos 5 and 12 (17- and 36-day-old nerves), in which the strength of the suture sites was considerably less than that of the intact nerves, the apposition at the suture sites was poor. In two animals (rabbits Nos 3 and 4) the strength of the sutured nerves (13 days old) closely approximated that of the intact nerves. This is in keeping with the histologic observations which in some instances (Figs 4 and 5A) showed structural continuity at this time. The degree of variation in tensile strength values of sutured nerves of a certain

age corresponded to the histologic differences observed at the suture site at the same age approximately. The variations seemed to result from differences in the type of apposition obtained at the suture line. The nerves appeared to

A



B

FIG 5—High power views of suture sites 14 days old. Microphotographs (A) taken from nerve in Figure 4 shows structural continuity which is not quite complete in (B) where macrophages are seen at the suture line (Hematoxylin and eosin,  $\times 150$ )

achieve a greater tensile strength value at a certain time when their ends were accurately coapted and well-joined. It appeared that the general condition of the animal too played a rôle in governing the rate of healing at the suture site

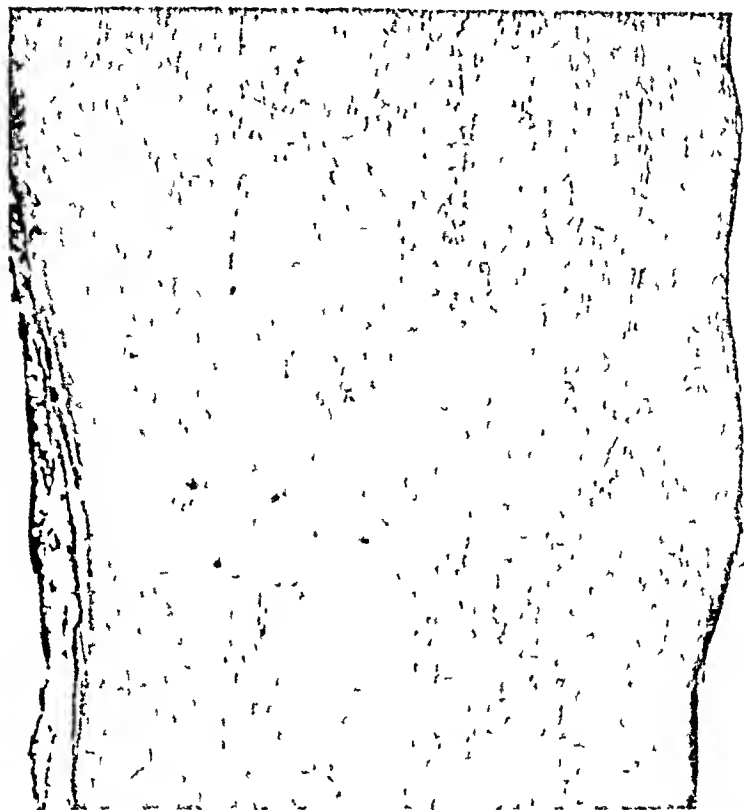


FIG 6—Nerve sutured with plasma clot and removed 18 days later. Structural continuity has been restored (Hematoxylin and eosin,  $\times 27$  )

TABLE I

SHOWING THE RESULTS OF TENSILE STRENGTH DETERMINATIONS OF BOTH THE INTACT SCIATIC NERVE'S AND ALSO NERVE'S SUTURED WITH AUTOLOGOUS PLASMA CLOT IN RABBITS

Tensile Strength (in Gm ) of							
Rabbit No	Sutured Nerve			Intact Nerve			Age of Sutured Nerve (in Days)
	Right	Left	Average	Right	Left	Average	
1	30	30	30	820	820	820	6
2	317	395	356	600	817	708	10
3	875	900	888	900	977	939	13
4	1 100	900	1 000	800	1,277	1,038	13
5	500	900	700	1 177	1 300	1 238	17
Poor apposition at suture site							
6	600	617	609	651	600	626	19
7	1 350	1,250	1 300	1 350	1 250	1,300	21
8	800	827	814	827	850	838	24
9	1 327	1 627	1,477	1,427	1 527	1,477	24
10	1,227	1,667	1,447	1,007	1,227	1,117	28
11	1,227	1,200	1,214	1,227	1,300	1,264	28
12	800	600	700	1,527	1,327	1,427	36
Poor apposition at suture site							
13	Withload of over 1,200 Gm nerve broke at point of application of clamp rather than at suture site			1 227	1,200	1,214	48
14	Withload of over 1,550 Gm nerve broke at point of application of clamp rather than at suture site			1 600	1 550	1 575	65

Rupture of the nerve following the application of a weight-load which was greater than it could hold, occurred at the suture line or, in a few instances, along the point of application of the clamp. At the suture site there was a fusiform enlargement amounting to 1–2 mm. In those cases where the strength of the sutured nerve equaled that of the intact nerve the stretch occurred to a greater extent along the nerve segment than at the suture site. The strength of the silk tension sutures removed at different intervals after operation showed considerable variation. After the age of 13 days they usually broke with the small weight-load of but a few Gm.

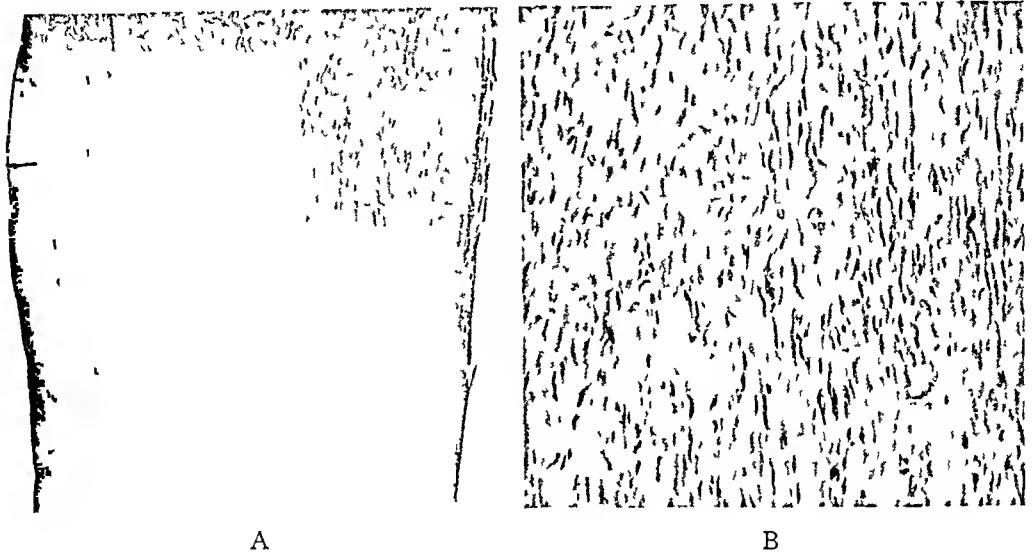


FIG. 7.—Nerve sutured with plasma clot and removed 30 days later. Complete restoration of structural continuity has occurred, including the regrowth of axon cylinders through the suture line. The suture line is free from inflammatory or fibroblastic reaction (Hematoxylin and eosin, (A)  $\times 21$ , (B)  $\times 150$ ). All photographs are from sections taken from dogs' sciatic nerves which were sutured with autologous plasma clot.

DISCUSSION.—The results of tensile strength determinations indicate that the rabbits' sciatic nerve of varying sizes sutured with plasma clot achieves the tensile strength of the intact nerve within a period of three weeks. That this statement holds also for nerves sutured with silk is rather suggested by the investigations of Miller.<sup>4</sup> Our microscopic observations in dogs indicate that this statement applied also to this species since structural continuity at the suture line was found to be complete at approximately this time. There is no reason to suppose that there might be any appreciable difference in the healing time of sutured nerves in man. It seems justifiable then to advocate the removal of plaster of paris encasements or other means of limb fixation three weeks after nerve suture and the institution of gradual extension of the joint at this time. These experiments indicate that there would be no danger of rupture of the suture site in well-made unions when a nerve is subjected to any strain three weeks after suturing. However, there is no doubt that there

is a limit to which a nerve may be stretched and yet remain capable of regenerating with resultant functional recovery of the innervated part. Highet and Sandeis<sup>9</sup> performed extensive resections of the external popliteal nerve of the dog suturing the nerve with the knee acutely flexed. Subsequent extension of the limb after a period of 14 days resulted in considerable histologic change apart from rupture of the suture site in some instances. The increase in length of the nerve following extension of the joint resulted from elongation of it whereas the straightening out of the tortuosity of the nerve played only a minor part. Rapid stretching in these animals did not produce any more damage than a more gradual stretching. The animal experiments of Denny-Brown and Doherity<sup>10</sup> demonstrated, likewise, that great damage to nerves accompanies transient stretches applied to them. Highet and Holmes<sup>11</sup> recorded cases in which lateral popliteal nerves were sutured with knees acutely flexed. The limit of stretch had apparently been exceeded in these patients since no recovery followed extension of the limb and microscopic examination of the nerves showed that they had been converted to fibrous tissue. It is a matter of common surgical experience, however, that nerves may be sutured with joints moderately flexed and good functional recovery result. However, the exact limit of nerve stretch that is compatible with satisfactory return of function can not at present be stated. Information is sorely needed on the results of nerve grafting and nerve stretching which are the only present alternatives to nerve suture with joints acutely flexed. Such data, together with information on the functional results following closure of gaps of varying sizes by end-to-end suture of nerves with joints flexed at different angles and then extended, is necessary in order to enable the surgeon to decide which procedure is likely to result in better recovery. The results of nerve grafting have thus far been disappointing, but with the use of the plasma clot technic for forming and suturing cable autografts<sup>12</sup> this method of grafting may yet prove of value.

#### SUMMARY

In a series of rabbits and dogs the sciatic nerves were cut and sutured with plasma clot and the nerves were removed at various intervals after operation. Combined microscopic observations and tensile strength determinations of the sutured nerves indicated that the tensile strength value of the intact nerve is regained approximately three weeks after operation and structural continuity at the suture line is restored at this time. It is concluded that in those cases in which joints must be flexed in order to perform end-to-end suture of nerves and the extremity encased in plaster, the encasement may be removed three weeks later without danger of rupture of the suture site during the subsequent extension of the limb.

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#### ANNALS OF SURGERY

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# BRIEF COMMUNICATION

## ENEMA TUBE PERFORATION OF THE COLON

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FROM THE DEPARTMENT OF SURGERY, PRESBYTERIAN HOSPITAL, CHICAGO, ILL.,  
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THERE ARE MANY REPORTS in the literature of perforations of the colon, some the result of the use of various types of enema tubes, others from the injection of fluids and air, and still others from the introduction of foreign objects. Fortunately, perforation of the colon by an enema tube or catheter, used in irrigation of a colostomy, is exceedingly rare.

Of the three cases reported, two of the patients sustained perforations of the colon at home. In the third case, perforation occurred while the patient was still in the hospital. The three patients had a terminal colostomy in the left lower quadrant of the abdomen subsequent to removal of the rectum for carcinoma.

It is common practice to irrigate the colon through a colostomy in the postoperative management of combined abdomino-perineal resections. In the vast majority of cases irrigations are accomplished without accidents, but, on rare occasions, undue force may carry the tube through the bowel. It has been suggested, however, that in some cases where there is a short mesocolon, an angulation of the bowel is formed, with the result that it is extremely difficult to get the catheter beyond the point of angulation. Repeated pressure of the enema tube against the angulation may result in pressure necrosis and perforation.

The clinical course is a rapid onset of pain, following the escape of the enema into the abdomen, with a rapidly developing peritonitis. Two of these patients were operated upon the day of perforation because of typical onset of symptoms. The third patient was not operated upon until three weeks following perforation. The enema apparently was placed into a walled-off pocket which prevented the escape of colon contents into the general abdominal cavity. All of the patients lived, and eventually were discharged from the hospital.

### CASE REPORTS

**Case 1**—O. S., male, age 77. This patient had a combined abdomino-perineal resection one year previously. He reentered the hospital because of abdominal pain of six hours duration, as the result of an enema administered into the colostomy. Examination revealed a surgical abdomen. Exploration demonstrated a small perforation in the medial side of the colon. The patient's postoperative course was uneventful. He was discharged on the 14th day.

**Case 2**—C. C., male, age 53. Six weeks after a combined abdomino-perineal resection the patient was readmitted to the hospital with what seemed to be a generalized peritonitis following an enema administered through the colostomy. At operation, a small perforation on the medial side of the sigmoid colon was found. Later, a large abscess in

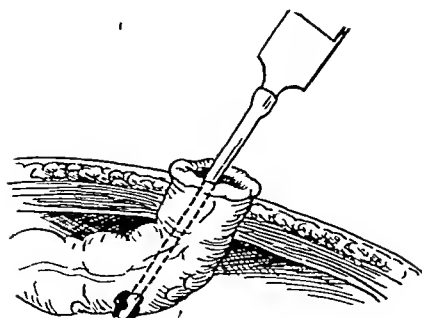


FIG 1—Case 1 Location of perforation in sigmoid colon

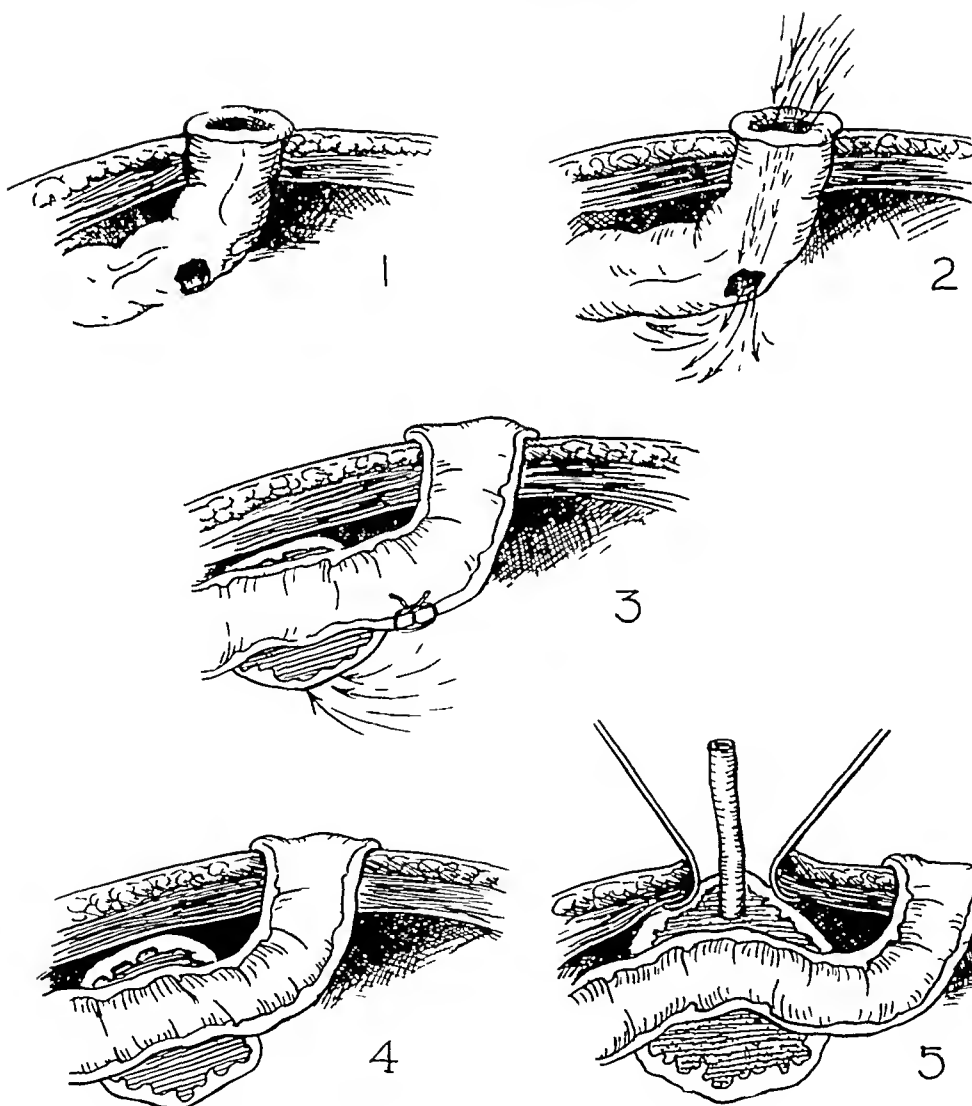


FIG 2—Case 2 Secondary abscess subsequent to suture of perforation

the region of the colostomy was drained. Following this secondary drainage convalescence was uneventful.

**Case 3**—F. Z., female, married, age 58. Two days after a combined abdomino-perineal resection an enema was administered through the colostomy, without any immediate abdominal distress. On the 4th postoperative day marked abdominal distention developed, associated with signs of a localized peritonitis. Decompression of the abdomen with a Miller-Abbott tube was carried out. Three weeks later an abscess was drained. Prompt recovery followed.

In the postoperative care of colostomies, Dr. Vernon C. David has used a technic that avoids the danger of perforation. This method suggests the use of a catheter which is placed through an inverted rubber nipple, similar to the type used on a baby's bottle. The nipple, with the catheter, is placed in the colostomy. This provides a water-tight compartment, so that when the enema fluid is injected the bowel lumen becomes distended. In this way the

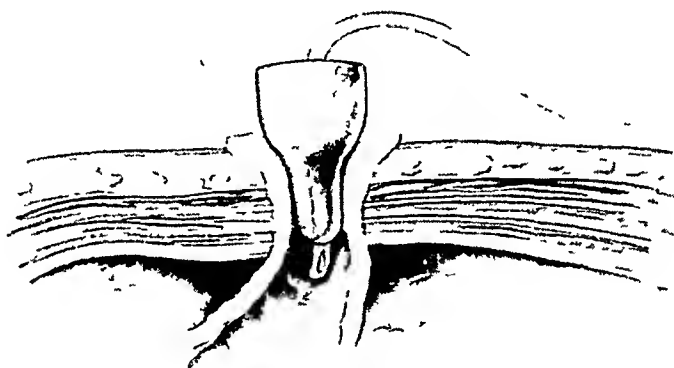


FIG. 3—A safe procedure for irrigation of a colostomy, as recommended by Doctor David.

catheter does not readily strike the wall of the intestine, and avoids pressure necrosis and perforation.

The lesson learned in these cases is the recognition of the danger from the use of an enema tube or catheter, whether it be in skilled or unskilled hands. Before a patient is permitted to give himself an enema he should be instructed carefully in the method of introducing the catheter into the colon. The practice of carrying the catheter any distance into the colon should be forbidden. A simple insertion of the tube into the colostomy should never be farther than the depth of the abdominal wall. This procedure is certainly the safest technic.

Many patients may use an enema tube through a colostomy for years without injury to the colon. However, we feel the rarity of the complication should not permit laxity on the part of anyone in the management of these cases. Residents, interns, and nurses should be cautioned concerning the danger of perforation in the postoperative management of colostomies.

## BOOK REVIEW

### DIAGNOSIS AND TREATMENT OF MENSTRUAL DISORDERS AND STERILITY

By Charles Mazer, M D, and S Leon Israel, M D 570 pages and 107 illustrations  
Paul B Hoeber, Inc, N Y

MENSTRUAL DISORDERS are among the most distressing conditions from which women suffer, and with which the physician must contend. When such dysfunction is associated with sterility in the married women it is one of the main causes of marital unhappiness.

To explain the reasons for physiologic dysfunction in the female and the causes which lead to sterility, Mazer and Israel succinctly describe in this volume the factors which play important rôles in the etiology and treatment of menstrual disorders and sterility. The normal physiologic menstrual functioning of the female depends upon the harmonious action of the pituitary, ovary and uterus. In order that the clinician and student may more readily appreciate the abnormal conditions from which women suffer, these authors appropriately preface their publication with a review of the anatomy and physiology of these organs.

A feature of each section is the authors' advice as to the therapeutic measures which, in their hands, have proved valuable. They present an evaluation of the medicaments usually used in clinical practice based upon their own experience or upon authoritative reports.

The section on amenorrhea is thoroughly and painstakingly well done. In the treatment of idiopathic amenorrhea and sterility, irradiation plays an important role and the authors substantiate its position as the correct mode of therapy, though they acknowledge, as do others, that "the *modus operandi* of low dosage irradiation of the pituitary gland and ovaries in restoring their functional activity and the menstrual rhythm is as yet obscure." But that irradiation does produce effective results is amply supported by their carefully supervised clinical experience. They too, note that irradiation when properly applied is harmless to both the mother and to the children born following such therapy. They appropriately call attention to the necessary caution, "one must, nevertheless, remember that in ovarian irradiation the margin between the harmless and the harmful dose is limited, and variation in dosage should for the present be definitely avoided. Therefore, only the skilled roentgenologist should be entrusted with this treatment."

Irradiation plays an important part in the treatment of uterine dysfunctions and in the treatment of fibroids, although this mode of therapy is not mentioned by the authors in the chapter on uterine fibroids.

This reviewer is not in accord with the authors' opinion regarding the treatment of menorrhagia with irradiation. In his hands irradiation has proved satisfactory in most instances.

More and more clinicians have come to realize that it is not always the female who is to blame for the barren marriage and that it is equally important to examine the husband for infertility. The section on male sterility by Dr. Charles W. Charny is excellent.

The appendix, listing in detail the commercial endocrine products available to the clinician, and the authors' evaluation of their worth, is an added aid to the doctor who treats menstrual disorders.

The book is well-printed and illustrated, the paper, exceptionally good. The authors' style makes pleasurable reading. All in all, it is a good book.

IRA I. KAPLAN, M D



## TRANSACTIONS OF THE AMERICAN SURGICAL ASSOCIATION

MEETING HELD AT HOT SPRINGS, VA  
MARCH 25, 26 and 27, 1947

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### ADDRESS OF THE PRESIDENT SCIENCE AND HUMANISM IN SURGERY\*

EDWARD D CHURCHILL, M D  
BOSTON, MASSACHUSETTS

"I will impart this Art by precept, by lecture, and  
by every mode of teaching"—Oath of Hippocrates

IN THE AUTUMN OF A D 9 the German hero Arminius fell upon Quintilius Varus in the shades of Teutoberger Forest and destroyed three of the finest legions of Rome. The bold victory forced the Romans to withdraw their frontier from the Elbe to the Rhine. This event brought down what now might be called an iron curtain between the Germans and the Graeco-Roman civilization. To imply that this curtain actually led to the development of a Germanic culture and science separate from that of the rest of Europe would be an error, for during many centuries wars and religious disputes swept across the entire continent of Europe, leveling cultural and scientific barriers. This very error, the concept of a separate Germanic culture, was partly a cause and somewhat a symptom of the rapidly moving events of the present century that culminated in the total destruction of Germany. Nevertheless, American Surgery as we know it today has developed from the union of two quite different streams, and the origins of these may be traced to opposite sides of this ancient iron curtain along the Rhine.

The stream from Germany was a turbulent freshet of Science, beginning in the middle of the nineteenth century and reaching full flood by 1914, now

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\* Address delivered before the American Surgical Association, March 25, 1947, Hot Springs, Virginia

nothing of its source is left but a dried-up watercourse. The broad river into which it poured had more distant origins in the ancient watershed of Graeco-Roman medicine, and reached the American Colonies from England and France. This was a leisurely moving current, rich in the humanitarian traditions of the Christian Church but, like the Church, burdened with dogma and superstition. Emergent leaders, from time to time, introduced scientific concepts of startling novelty and import, but the potential power of a new Medicine guided and nourished by Science had not been envisioned.

The junction of the freshet of Science with the broad and ancient river produced currents and countercurrents in American Surgery that are still visible today. Had the content of Surgery been pure Technology, on the one hand, or pure Science, on the other, the mingling of the streams would have occasioned no disturbance, the contribution of the Germanic freshet would have been received quietly into the volume flow of the river. To understand the troubling of the waters, it is necessary to examine Surgery closely and define its content and its function. It is also necessary to consider the organizational patterns through which its content is converted into dynamic function. First I shall consider what may be called the Content of Surgery.

Surgery is in large part a handicraft with elaborate technics that may be grouped as Technology. But it transcends Technology in the desire and responsibility to find safe application of these technics to the needs of humanity. This quality, which distinguishes a profession from a trade, may, for lack of a better term, be designated as Humanism and identified as one of the basic contents of Surgery. Historical documentation might be required to convince certain purists that Surgery can rightfully identify another of its component parts as Science. As the argument would require precisely drawn definitions, I shall not belabor the issue but boldly stake out a claim and defend it, if necessary, at some future time. In addition, if one be honest in this analysis, he cannot fail to see that Surgery is seeded with *ad hoc* hypotheses, or, in more frank terms, empiricisms and irrational beliefs. These four components, Technology, Humanism, Science, and Empiricism, form what may be called the Content of Surgery. This differs from the Content of Internal Medicine only in the greater range of surgical Technology.

In common with all professions, Surgery expresses itself in Dynamic Functions. These, considered broadly, are three in number: Cure of Disease (action), the Strengthening of the Skill to Cure by Progress (growth),\* and the Perpetuation of the Skill to Cure by Teaching (reproduction).

The Content of Surgery is transformed into the Dynamic Functions of Surgery by means of various Organizational Patterns. These patterns, at least in recent times, have been various combinations of the Hospital, the University, and the State—including in the State, agencies within the framework of

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\* I have deliberately avoided use of the term "research." Progress in surgery may result from a wide range of effort that extends from the employment of common sense and logical thinking to the use of the well-controlled experiment designed to answer a precisely formulated question.

government and agencies designed to administer social forces independent of government

Having dissected Surgery in this arbitrary manner in an attempt to bring some clarity of thinking to the subject, I shall turn to the historical approach, and choose examples chiefly from Teaching. Major trends in surgery that alter the relative emphasis placed upon those abstractions that I have called its Content are foreshadowed by changes in Teaching. The reason is obvious, because only an oncoming generation has sufficient weight to shift the emphasis to a significant degree, furthermore, the teachers of any profession are likely to be sensitive to an approaching change and, being articulate, herald its approach. The pursuit of this cockcrow responsibility by teachers always has annoyed the profession at large. But medical education will remain a controversial subject just so long as Medicine itself is open to change.

In selecting examples from the history of Teaching, I have chosen ones that will record the advent of Science and also certain ones to reveal the content of Humanism that resides in Surgery. The controversies, as usual, have not dealt with basic problems, but have centered on organizational patterns, particularly those formed by University and Hospital. These patterns are unimportant in themselves, they achieve significance only as they succeed or fail to transmit with fidelity the total Content of Surgery. The University is selective in its response to the wave lengths of Science, the Hospital is selective in the expression of Humanism. In view of an ever-changing Content, it is not surprising that a perfect instrument as yet has not been achieved.

The Germanic influence in American medical education was not apparent until the rise of scientific medicine in Germany in the middle of the 19th century, and so a background must be sought in the situation in Britain during the 17th and 18th centuries.

Only a beginning was made in 17th century Britain to displace the entrenched classicist methods in medical education.<sup>1</sup> The traditions of Oxford and Cambridge were essentially conservative. Medical studies at Cambridge were governed by the Elizabethan statutes of 1570. The Caroline Code of statutes was instituted at Oxford in 1636 and strictly regulated medical studies at that University. Oxford was permitted to grant a surgeon a license to practice throughout England after he had shown "skill, honesty and repute in that art" for seven years. "He must have performed two anatomies, made at least three cures and been approved by three doctors of the University, or by the Regius Professor and one other doctor. Upon graduation he promised to cure four paupers gratuitously and not to overstep the bounds of his own art by attempting to practice medicine. Furthermore, he gave his word that he would 'not ask too much salary, or delay any cure with the view of later gain'."<sup>2</sup> The efforts of the universities in medical education were not looked upon with favor by the great practitioners of that day, who taught the art by the apprentice system. "Physick," says Sydenham, "is not to be learned by going to universities, but hee is for taking apprentices, and says one had as good send a man to Oxford to learn shoemaking as practicing physick."<sup>3</sup> "A



Doctor bred up in the Contemplative Philosophy of the Schools, may be a Scholar and a very fine Gentleman, but what is that to the curing of a Disease, or the rousing of a Heart-sick Man from his bed of Languishment?"<sup>4</sup>

Compared to that of the universities, the situation with respect to hospitals was even worse. The action of Henry VIII that swept away the medieval hospital system of England in the name of the Reformation has been interpreted as an effort to abolish the extravagances of the ecclesiastics. Whatever the motive, this harsh decree was followed by a period of misery and confusion that lasted nearly two centuries. Then a new philanthropy was born that was destined to express itself through a practical and concrete charity and bring a new concept of the hospital to the world. Whether or no the panic of the Great Plague was immediately responsible, there came a "revival of charity with all the old touch of romance which characterized it in the Middle Ages."<sup>5</sup>

The Crown first tried its hand in the new philanthropy, but its benevolence was inadequate and the administrative control measures it established proved harassing. Then in the 18th century came the magnificent rise of the voluntary general hospital that formed the pattern for the first hospitals of our new world.

The first organization of medical teaching in this country took place in Philadelphia in 1765. John Morgan (1735-89) had been recommended by John Fothergill, a physician of London, as being qualified to teach. Morgan, a graduate of Edinburgh in 1762, had worked under William Hunter and the Munros. In a letter to John Warren in 1785, Morgan showed an awareness of the significance of the medical sciences, that were then but weak, ancillary forces in education. "Medicine," he stated, "is a science as important in its object as it is difficult in the acquisition. It is very extensive in its researches, and presupposes the knowledge of many other sciences. The cultivation of it requires no small abilities, and demands of those who engage in the arduous pursuit an enlarged and benevolent mind."

But there were too many pressing problems in the days of the Revolution to give time to the cultivation of the science of medicine. Morgan himself, in 1775, was appointed "Director General and Physician in Chief" of the American Army. Packard, in describing the Army medical service of those days, writes "The surgeons were without any definite authority, absolutely destitute of any medical or surgical supplies, except those provided by private means, and in many cases as ignorant and ill-educated men as could well have been found." According to Garrison, Morgan "entered upon his duties with vigor, insisting upon rigorous examinations for medical officers and subordinating the regimental surgeons to the hospital chiefs." But the politicians, both professional and lay, soon had his head and he was dismissed by Congress in 1777.

The early medical schools merely supplemented the training given by the apprenticeship method. The courses of lectures were only nominally under university control, and although dignity was sought through the sanction of a university, they existed wholly for the interests of the professors. "Students in small classes of two or three lived in families of surgeons, studied methods, followed their cases, compounded their drugs, did their chores and received a

certain amount of personal instruction"<sup>6</sup> The pace of learning was slow and the ultimate attainment not great, even though eventually the apprentice might absorb all that the instructor had to offer

During the last century many of the developments in this country were shaped by the rapid expansion of population in a tremendous geographic territory As a result of the demand for doctors, the inevitable happened "Loose and shifting bands of practising physicians, calling themselves a faculty, tried to impart, chiefly by lectures, to heterogeneous, uneducated groups of students the empirical knowledge—sound and unsound—which they themselves possessed First and last, American towns have produced over 400 such medical schools The teaching of medicine on these terms was, directly, in cash, and indirectly, in prestige, a profitable business"<sup>7</sup> Proprietary medical schools have been defined by Zinnser as "privately founded corporations of groups of physicians and surgeons who organize courses without a well-conceived educational plan"

Henry Jacob Bigelow was appointed Professor of Surgery in 1849 He had studied long in Paris and had journeyed weekly to London to hear Paget In accordance with his time, he deemed the didactic lecture paramount The operating room was the theater in which he excited the astonishment and admiration of his students Bigelow has been introduced at this point as a concession to chronology I will leave him busy with his didactic lectures—unaware of the floodwaters that were arising in Germany, destined to descend on the well-regulated little world of surgery that was so firmly under his control

The story begins in Germany during the last years of the 18th and the first decades of the 19th century, when German philosophers—particularly Kant (1724–1804) and Schopenhauer (1788–1860)—provided a powerful impulse to science in the universities of that country "That was a most resplendent epoch, but so little was it a function of a certain people or race that it passed, it passed like the Hellas of Pericles, the Italy of the Renaissance, the France of Louis XIV human history makes efforts like these, in which a flowering of men of genius comes to the world, only at intervals of centuries or millennia"<sup>8</sup> Philosophical thought was already declining by 1830, but the united and imperial state fostered a period of industry and achievement in German universities that flowered in research in the natural and medical sciences The wealth and importance of Germany's intellectual and technical achievements made it a country to which our students turned as the fountain-head and guide of medical science This was, in all, a brief period, 1850–1914, but its impact on medicine and medical education has been enormous To trace the effect on American medicine, I shall sketch the career of one of the first American students to enter Vienna, Dr James C White

In 1853, four years after Bigelow became Professor of Surgery, J C White, of Belfast, Maine, started his course in medical studies To complete the background it is necessary to hear his own story about the medical studies in Boston that prepared him for his work abroad<sup>9</sup>

"Coming from the preparatory fitting of the public school or academy, or

from college, the medical student of those early days had but small choice of medical schools from which he might receive his professional degree. This might be acquired, by entering his name with some physician and purchasing professor's tickets at two winter courses of lectures, in two years' time, after a final and farcical examination. These were the minimum requirements to turn a rough country boy into a doctor authorized to practice medicine in those days. There was no obligation to attend a single exercise during the medical school course of lectures lasting three or four months, or to receive any manner of instruction from his nominal instructor during the remainder of the year.

"What did Harvard University offer the student of medicine at that time? Its Medical School consisted of seven professors. They had entire control of the affairs of the school. They sold their individual tickets of admission to their respective courses through a business agent, and every candidate for a degree was obliged to buy them all for at least one year. The purchase of a similar set of tickets in any other reputable medical school was accepted as the equivalent of a second course of lectures at Harvard. The exhibition of a certificate of having entered one's name three years previously with some practitioner, the preparation of a thesis on some subject in medicine, and answering the simple questions put by each professor in turn for seven minutes each, equal to a total of one and a half hours, constituted the only and final method of examination as to the fitness of a candidate for a degree. If he received the favorable votes of a majority of the board—four—he became a Doctor of Medicine, and that degree carried with it authority to practice in Massachusetts. The lectures began at eight in the morning and continued until one o'clock, five consecutive hours on some days of listening for the conscientious student without interruption save for the five minutes' intermission between them. They were repeated without change each year. Twice a week there was a clinical medical visit at the Massachusetts General Hospital of one hour, which the whole class of 127 students attended filling the ward—of whom but 31 held a college degree. On Saturdays there was a similar visit in the surgical wards, followed by operations in the amphitheatre under the dome for an hour or two. There was no graduation of studies, the whole body of students attending each lecture from first to last together. There were no laboratories, no private courses, no individual instruction—no student looked into a microscope or handled a test-tube."

Having completed his medical course in the spring of 1856, young White was obliged, if he desired a more adequate education, to seek it abroad. His decision to go to Vienna was an important event, how he came to make it is of interest.

"Paris had long enjoyed the reputation of holding the highest rank as a school of medicine, both in her renowned teachers and the clinical advantages she possessed. But a change was beginning. Gradually the philosophic German mind, so skeptical and irreverent as to accept no dogma unchallenged, and so patient and industrious in following the suggestions of nature to their

source, began to make itself felt. This influence soon became an acknowledged power as the careful observation of devoted students—men who cared for nothing else in life than their studies, who had no higher ambition than their scientific reputation, who knew no other pleasure than was to be found in the laboratory or hospital, and who never aspired to become rich — became known.

"Dr. Calvin Ellis, just returned from Europe, had spent a few weeks in Vienna and advised me," writes White, "to make it my first and chief place of study." At that time few American or English medical students visited Vienna. I was the first of the former, I believe, to spend a full year there, and there were but four or five others during my residence there, for the fame of its incomparable teachers had scarcely spread to America or England." So in August, 1856, White embarked in the *City of Washington*, a ship-rigged, side-wheel steamer, running between New York and Bremen, and after 14 days arrived at the latter city.

As I am concerned only with the broader aspects of changes in medical education, it is beyond my purpose to record the detailed history of the reforms of the last half of the last century. Adequate illustration is afforded by following Doctor White after his return from Vienna. In 1866 editorials from his pen appeared in the *Boston Medical and Surgical Journal*. These were regarded as rank heresy by his colleagues, and he was advised to restrain his zeal.

"Not until the profession throughout the country," he wrote, "shall awake to the deplorable deficiencies of our present system and shall insist upon the establishment of some uniform standard can medicine in America raise itself to a level with that of foreign countries, or even with other branches of learning at home.

"Very little can be accomplished in this direction by any one school, however desirous its government may be of reform, for any unusual severity in its examinations or length of study required would turn its students to other and easier places and prove its own ruin. How far, for instance, would the cause of medical education be advanced if Harvard University should refuse a degree until after four years' study while the Medical Department of Yale College continues to confer the same right to practise at the end of two years only, and issues a circular containing such a statement as this: 'Experience has shown that a large proportion of the whole field of medical investigation, embracing most of the important topics, can be comprised in a single course of lectures, by avoiding that extreme variety of subjects and minuteness of detail which are so apt to confuse and oppress the mind of the learner, and render the knowledge acquired superficial and vague, rather than clear, definite, and well fixed.' When an institution of this rank so lowers the tone of scientific study, what can we expect of the great number of private schools all over the country licensed to make doctors by State Legislatures?"

In 1870 Doctor White, then a distinguished member of the Harvard faculty, delivered the Introductory Address at the opening of the winter course

of lectures "President Eliot, who had recently been appointed to that high office, to whom I read my address in advance, said he would take measures that I should have a good audience, and so at noon on November 2, I found the large lecture-room of the Medical College filled with the students and many members of the governing bodies of the University. The invited guests assembled in the Warren Museum above, and there Professor H. J. Bigelow said to me 'Well, White, now we are about to catch it, I suppose'."

The address itself will bear reading and rereading today, and time allows but limited direct quotation.

"To those who have received no advice upon these matters I would say, devote the largest part of your time to anatomy, physiology and chemistry.

These branches are the groundwork of the art of medicine, and it is in these that students generally fail in thoroughness, and therefore as physicians fail to know their art through life.

"By such beginnings you will gain the taste and courage for that independent work in later years which will distinguish you from the ordinary practitioner. I do not mean to say that you should take absolutely no share in any of the other exercises of the school, that you should not attend operations and occasionally visit the hospital, and see an autopsy, and perhaps study surgery and materia medica, but the less of these and the more of the others the better. A single year's attendance upon the advanced branches after such a preliminary training will give you a far deeper knowledge of them than one gets by a three years' course pursued without system or given wholly to the so-called practical or special branches."

"There is no such contemptible spirit among students as preferred attention to such parts of their studies as seem to have a practical value. It exhibits itself in attendance upon the lectures relating to the practice of medicine in the production of the note-book only when the word 'treatment' is mentioned and in the neglect of all that raises medicine to the rank of a science and its followers to be learned men. It degrades the art to the level of a mere trade."

"nine-tenths of all that is new and important in physiology, pathology, and medical chemistry, is the work of German hands and brains, and is given to the world in their tongue."

"So long as it is held that there is a demand for cheap doctors in this country so long we shall make poorly educated doctors and nothing else.

"Until we renounce the theory that medicine in America is to be taught, not as a science as elsewhere, that only so much of it is to be served up to the student as will make him a good practising doctor, and that he has no share in its future progress as an independent worker in its deep places, we need not hope for better things.

"We do not sufficiently honor our own calling. We labor mainly to acquire position and comforts, but how few of us are really students and care more for the advancement of science than for our own 'getting-on' in the world.

How seldom has an American physician made independent and systematic investigation in any of the sciences connected with medicine!"

White describes in his memoirs the effects of his attack on contemporary medical education "This address was followed by the most lively agitation in the faculty Finally the scheme of the reformers was adopted (1871) By this hard-fought victory the school made a nine months' course compulsory, adopted a graded curriculum extending over three years, and obliged candidates to pass a written and thorough examination in every one of the great departments of medicine" Surgeons today will forgive him for a final shot directed at the venerable Henry J Bigelow "My own examination in surgery at graduation was the question, 'Well, White, what would you do for a wart?'"

But Bigelow was not silenced, and rose in defense of the educational policies of the old school at the Massachusetts Medical Society<sup>10</sup>

"It is plain," he said, "that the mass of work must be performed by the practitioner, who has been educated with the view of turning his acquirements to immediate practical account, and whose business so occupies him that he contributes comparatively little to the absolute advance of knowledge You are to provide 50 such plain and competent men for one who knows more"

"These remarks are not intended as a plea for mediocrity It should be remembered that our present system of medical education, imperfect as it may be, produces men eminent in science, and furnishes able teachers as well as distinguished practitioners Most eminent men are in a large degree self-made, and have pursued their subject from the attraction before them, and not from a stimulus behind The material out of which philosophers are made is largely supplied from their own intrinsic and determined will Genius is talent with a strong driving power You cannot create this talent You may, indeed, give it opportunity, but you cannot force it"

"Whatever else it may or may not do, a medical school should aim first, then, to give a plain, sound, solid education, without error, if without ornament"

Although Bigelow was outvoted in the University, there was a redoubt to which he could retreat—the voluntary hospital, in which his word in surgery was supreme Universities were quite remote from the voluntary hospitals of 1870 and, in fact, to this day must tread with caution within their portals

The Voluntary Hospital,\* as an institution, has fully as ancient a lineage as the University, for the germ of the hospital system existed long before the Christian era The Greek and Roman temples resembled "clinics" more than "churches," and their priests were well versed in medicines The history of the hospital movement is a long and romantic story, but "undoubtedly the greatest event in the history of the hospital movement throughout the world was the coming of Christ at the very moment that the Roman Empire had united all

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\* There have been in this country many integrations or actual mergers between voluntary hospitals and universities, and in some instances between voluntary hospitals and government, either state or municipal Also, many large municipal and state hospitals have developed after the pattern of voluntary hospitals

the Western nations into one vast civilization"<sup>5</sup> With Christ came the concept of Charity

This great motivating force, the desire to relieve suffering on its own merits and for its own sake, became the soul of institutions destined to evolve into the voluntary hospitals of the Western World—at the moment the iron curtain was descending along the Rhine. Professional historians must assume responsibility for tracing the evolution of these institutions through the devious pathways of the Middle Ages, the Renaissance, and the Holy Roman Empire. The fact remains that at the opening of the 19th century, medicine and medical education in Germany were found within the University and incorporated into the framework of the State. Medicine and medical science thus received a direct stimulus from university philosophic thought, and aided by the financial support of the State, entered its productive period of scientific advance.

In England and in America there had been no recognition of a duty of the nation to the sick, "except in so far as they become a danger to the community, like the ancient lepers." The care of the patient was centered in voluntary hospitals, separate from universities and outside the framework of the state. English hospitals had established their own schools of medicine, a development copied in this country but to a limited extent.

The sincerity and idealism of the Voluntary Hospital cannot be written off as self-interest and bigotry, as some have tried to do.\* In 1886 Henry J. Bigelow was again voicing his wrath, but at this time against a force that was striking at the soul of his voluntary hospital. In an open letter<sup>11</sup> he warned the Trustees of the Massachusetts General Hospital that "some members of the Staff have a desire to use the institution to their professional emolument. In my opinion any such changes, however plausibly introduced, will inaugurate for the Hospital an era of decline. Its Trustees should weigh carefully any measure which would tend to confuse the administration of a great public charity with the promotion of private interests."

Charity in the literal sense and in the form of alms dispensed by Lady Bountiful may disappear from the American scene, but the medical profession would do well to treasure such vestiges of it as remain. Charity in the material sense is symbolic of Charity in the broad spiritual sense—the desire to relieve suffering for its own sake. This is the compelling force of Humanism, that I have placed with Science and Technology in the basic content of Surgery. Charity in this larger sense is the most precious possession of Medicine. As motivation for the physician it has been closely entwined with teaching and research. It is expressed in his basic rules of ethics and determines the privileges and trusted position of the physician in the social order. The foundations of the Voluntary Hospital rest upon this great concept of Charity, it is found in the blood and sinews of these institutions today. It is without exact coun-

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\* "Conservatism, vested interests, absence of true university ideals, lack of resources, lack of leadership and excessive dependence on tedious committee procedure." "Staffs, huge, unorganized, unpaid, unassisted, had been put in charge, appointments went variously—by political pull, by personal favor, occasionally even by merit."<sup>7</sup>

terpart in the traditions of the University, it is far too intangible to be codified by the State

I have tried to show that up to 1870 medicine and surgery in the Graeco-Roman-Franco-British-American stream were pursuing a steady but slow evolutionary trend "There was no sharp line between the practising and the teaching profession. The practitioner taught—and, if he pleased, investigated." From this stream even then was emerging Lister and, before him, Claude Bernard, Louis, Bright, Laennec, Charles Bell, Jenner, the Hunters, Sydenham, and William Harvey. Flexner, in referring to leaders of this type, states that "their situation and environment instead of helping, progressively impeded them." It would be of more interest to learn what happy combination of circumstances led to their appearance.\* By 1870 floods of specialized knowledge and technics were bursting forth from German and Austrian universities. The proposal of the youthful President Eliot to change medical education was supported by the members of his faculty who sensed the situation. Although the position of the preclinical departments of the Medical School was strengthened and the curriculum graded and extended, what might have been a major effect upon medical education was attenuated by the fact that clinical teaching was centered in voluntary and municipal hospitals, outside direct university control. No thought whatsoever was given to the postgraduate period of surgical education, that remained unorganized at the apprentice and private assistant level.

The story of the opening of the Johns Hopkins Medical School (1893) is known to all students of medicine. But here I shall narrow the focus to surgical education at the postgraduate level. In designing the surgical clinic at the Hopkins, Halsted duplicated in so far as possible the pattern of the German clinics. "It was our intention," he stated, "originally to adopt as closely as feasible the German plan, which, in the main, is the same for all the principal clinics of the German universities. The house surgeon, or first assistant, as he is called in Germany, is selected, after several years of service, from a number of well-tried assistants. There is no regular advancement from the bottom to the top of the staff of resident assistants. Only a small proportion of these venture to entertain the hope of becoming first assistant. Occasionally an assistant from another clinic may immediately, or almost at once after transfer, succeed to this position over the heads of those who have served many years. This admirable system, which undoubtedly has

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\* In his President's Address, American Society for Clinical Investigation, May 2, 1927,<sup>14</sup> Eugene DuBois gave a critical and pessimistic account of the situation and environment that had been established in this country, as of that date, supposedly to nurture scholars of this stature. He posed the question of how a young Harvey or Laennec might fare in twentieth-century university medicine. In answer to his own question, DuBois decided that these gentlemen "after a good look at the present conditions would realize that they would be happier in their own small, inefficient but comfortable centuries. Harvey would beg to be returned to the England of James the First, Laennec to the France of Louis the Eighteenth."



its disadvantages, is possible only in a country where like conditions prevail and a close affiliation exists between the universities or where some great inducement exists for the making of assistants of the highest possible order. The professor of surgery, or the surgical chief, desires to secure as his first assistant or chief of staff, a man of great promise, not only because of the obvious immediate advantage to the clinic, but because such an assistant is likely to have tendered him, ultimately, the chair of surgery in some smaller university. It is a matter of great satisfaction and pride to a professor of surgery to have supplied from his staff one or more university chairs.<sup>12</sup>

The new experiment at the Hopkins was eminently successful. Halsted himself was a thoughtful and productive scholar. There was gold to be extracted from the medical sciences that fringed on surgery, and their technics of anatomic dissection, histopathology, and taxonomic bacteriology were readily acquired. Surgical Technology was being developed and modified at a rapid pace in full exploitation of the discovery of antiseptics by Lister. Halsted's hope that his able pupils would be called to chairs of surgery elsewhere in the country was fulfilled.

With an energy and enthusiasm typical of America, the experiment, started on a modest scale in Baltimore, was soon repeated throughout the country. New university clinics were created on the strict organizational pattern described by Flexner.<sup>7</sup> The blueprints were drawn in detail and the specifications written with precision. Nothing was left to a "gentlemen's agreement." The full-time system in clinical surgery was to "abridge the evolutionary process by setting up summarily the conditions necessary to scientific development on the clinical side."

There can be no doubt that the remodeling of American surgery was badly needed, there is no doubt that it came at a critical time. It helped close the gap between the discoveries of the laboratories of medical science and the clinics, as it was designed to do, it came at a time when the elaboration of surgical technics had opened the field for a gold rush in the pursuit of surgery as a trade. Successful practitioners scrambling for the prestige of a professorship all too frequently were preoccupied with large practices and with tastes similar to those of their friends and patients—the "robber barons" of commerce and industry. The public charity of the days of Henry J. Bigelow came to be referred to as "exploitation of the profession."

But the assumptions and conditions underlying the introduction of the full-time system as an attempt to quicken evolutionary processes, must clearly be recognized. The rapid expansion of the university hospital system called for a considerable number of physicians and surgeons to fill important posts. Flexner mentions this problem. "Will medicine," he asks, "enlist in its service as devoted, enthusiastic, and self-forgetful workers as have been absolutely essential to the development of other sciences? Or will physicians and surgeons crave conditions that the university cannot create or maintain?"

What kind of men were these German professors that it was sought to emulate? J. C. White described them. He tells us that "in Germany the

celebrated physician first makes for himself a name of incessant toil and self-sacrifice. He cares neither for society, for appearances, for comfort, only for science." Even more vivid is his description of an individual: "Oppolzer comes in punctually. I cannot give my first impression of him. It was, perhaps, that his pictures belie him, that he had made a very hasty toilette, had forgotten his collar, and had not made the same use of the Danube as we do of the Cochuatate. We may pardon the want of neatness, when we consider the low rank in social life to which scientific men of Austria are condemned."

That the organizational pattern be considered all-important is a familiar American tendency. Here even Flexner had reservations: "A full-time organization will not transform a sterile clinician into a proper university professor. . . it will not produce ability and enthusiasm where they do not exist, it will not make the sterile clinician fertile." There is evidence that Halsted fell into this trap. "Why," he asks, "was Germany the country first to adopt antiseptic surgery? Why did almost every surgeon in every German university eagerly embrace Lister's system almost at the same moment? The answers to these questions are, I believe, to be sought mainly in the character of the scientific training of surgeons in Germany." Therefore he set up an identical training schedule. Wouldn't it have been more pertinent to have asked: Why did Mr. Lister, FRCS, Eng. and Edin., who commenced a course of Lectures on the Principles and Practise of Surgery on November 7, 1855, and helped Mr. Syme in his consulting rooms on Rutland Street—why did this Mr. Lister *discover* antiseptic surgery?

It may be noted also that the organizational pattern chosen for transplantation had already started to deteriorate. Flexner admits that "in Germany during the last 30 years, despite the firm academic anchorage on which I have dwelt, the successful professor of the clinical subjects has time and again drifted away from his clinic and his laboratory. In recent years many university professors have established private clinics, managed as business enterprises. Thus the professional preoccupations of clinicians make sad havoc with professorial duties." This has a strangely familiar sound today.

In 1947 we have a larger perspective of the structure of German medicine than was given to those who so enthusiastically brought its pattern home to our shores. The last twenty years have shown how fragile was its bloom and how shallow were its roots. German medicine went down with the state through degradation to destruction. It has been profoundly disturbing to think that the medical profession, as individuals, shares the responsibility and to learn that in some instances individuals actually participated in the conspiracy.<sup>13</sup> Medicine was powerless to act in behalf of the humanity it should have been serving or to raise its voice to check the downward trend. The same was true of the Universities. In the shameful history of the Nazi conspiracy there was no happening more tragic than the failure of the Universities and of University Medicine to utter a word of protest. Was it solely because of their position within the framework of the state? Or had Medicine, neither pure

Science on the one hand, nor pure Humanism on the other, made itself vulnerable in Germany by neglecting Humanism in the pursuit of Science? Science is but one of the four components in the Content of Medicine

There are, of course, many secondary forces in this troubled stream of Surgery that have created their own whirlpools and eddies. These may be external, shaped by the social order, or internal, derived from Surgery itself. An example of the former is the complex structure of medical economics within which surgery is regarded as a trade. I have shown how the trade interest of surgery appears and reappears in relation to teaching, research, and the care of the patient. It has been encountered in the Hospital and in the University. It is a dominant factor in problems now vital to the State, such as the maldistribution of specialists and the spiraling cost of illness.

The trade interest of surgery now has relatively little influence on undergraduate medical education, for this is sheltered under the wing of the University. It is definitely shaping graduate education, so important in the training of the surgeon. The spread of "Halsted's resident system," established to further science and education in surgery, has found great impetus in the need of present-day hospitals and clinics for many young and willing pairs of hands. Exploitation of these hands by neglect of the minds and ideals that must be developed to guide them will repeat the evils of the undergraduate proprietary schools of the last century, when "the teaching of medicine was, directly, in cash, and indirectly, in prestige, a profitable business."

With better basic education, it should be found possible to shorten, rather than necessary to lengthen, special technical training.\* The dangerous gospels of force and uniformity are being spread in this critical area of adult education in support of organizational patterns originally conceived as aids to science and teaching, but developed in many instances as "training without a well-conceived educational plan." The time may not be distant when government will wish to take a hand and freeze in compulsory law the structures of graduate training that are being erected. It would be unfortunate were this to happen before these structures have been tested by further experience. In fact, this period of adult education is far better left entirely outside the law. But it would be well to remember that the interval between the reform in undergraduate education and the incorporation of the reform into law by the state was brief. It is but a short step from dictatorial certifying boards within the profession to proscribing boards within the law.

An example of a secondary force arising from within surgery is the fragmentation that has resulted from specialization. The origin of a specialty is usually traceable to a concentration of effort inspired by a desire to extend the scope of surgery by progress. Too often, however, a specialty has been perpetuated as a watertight compartment with emphasis on the mystic rites of technology and neglect of further progress, and ultimately there appears an unmistakable intrusion of the interests of the trade.

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\* Wartime experience has shown in many fields that it is possible to train men faster than had been supposed.

This brief foray into medical history has shown the need for new soundings in the onrushing stream of Surgery. On the one hand, it is time to face facts and agree that increased emphasis upon Science has resulted in progress that has guided Surgery out of medievalism and established the benefit of its skills as one of the rights of humanity. No longer could a Henry VIII or any other ruler close the hospitals of a great nation. It is also evident that the "reforms" of the last 70 years came at a critical time when the self-interest of surgery as a trade, armed by a great expansion of Technology, might have been a real threat to the functions of teaching and progress.

On the other hand, the opposition to the reforms that were introduced brought forth criticisms that were not entirely expressions of unenlightened self-interest, despite the fact that many local episodes of bitterness and conflict are traceable to encroachment on the monopoly interests of trade. There was something deeper—an inarticulate and sincere concern lest the dazzling light emanating from Science eclipse that other content of Surgery I have called Humanism. The humblest member of the profession is vested with the right and the duty to enter his protest against such a threat, for the obligation written into the Hippocratic Oath makes every practitioner of the Art share responsibility for Teaching. "I will impart this Art by precept, by lecture, and by every mode of teaching." This is an obligation unique to our profession.\* While teaching in the literal sense may be delegated to a limited group, responsibility for the preservation of balance in the Content of Medicine rests on the profession as a whole, and not on some chosen segment that might veer like a weathercock with every change of wind or on some other occasion remain fixed long after the prevailing wind has changed.

Surgeons are men of practical affairs and tend to be self-conscious about a direct expression of the ideals upon which their profession rests. But what I have said has been said many times before. It is found in the writings that inspired and guided the growth of the Voluntary Hospital. It is found in the essence of what is called Western Civilization. It was set down long ago in very simple words: "And though I have the gift of prophecy and understand all mysteries, and all knowledge, and though I have all faith, so that I could remove mountains, and have not charity, I am nothing."

This, I believe, is the real warning Medicine gave to those enraptured by German Science. Medicine is too close to the needs of humanity, and is too loyal a friend of mankind in times of fear and trouble, to cast aside abruptly its heritage of Christian ethics for what has been called the "moral irresponsibility" of Science. The future of Medicine and very possibly the future of Science itself will be determined by the wisdom and kindness with which the great gifts of Science are assimilated and made available to human needs. "I do not know," writes George Sarton, "who is the poorer

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\*True, great teachers of mankind have expressed little concern about who should carry forward their precepts. Just as Hippocrates spread the responsibility for teaching to all of his disciples, so did Christ. Later the successions of Professors and Popes appeared with delegated responsibilities for the perpetuation of organized experience (and dogma).

the old humanist without understanding of science, or the scientist without reverence I do not know which is worse idealism without knowledge, or knowledge without idealism We need both equally in order to go forward and prepare the dawn of a new age .<sup>15</sup>

There can be little doubt that Surgery is facing further change in the relative emphasis placed on the component parts of its content Science will increase, and scientifically based Technology will slowly replace Empiricism There are certain to be changes in the organizational patterns formed by Hospital, University, and State These changes may be brought about by explosive forces in the restless external social order, or anticipated by a sensitive government Change is to be feared only if those responsible for the preservation of essential values falter in their task In fact, change is welcomed in so far as it may strengthen the profession to meet the new challenges that confront our civilization

In times of change there is need for wisdom both in the external social order and within the profession Spokesmen who loudly proclaim measures based on self-interest will not be tolerated A hold-fast in Science is essential, but this represents only a part of the strength of Surgery By maintaining the ancient bond with humanity itself through Charity—the desire to relieve suffering for its own sake—Surgery need not fear change if civilization itself survives

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# GASTRO-ESOPHAGEAL RESECTION AND TOTAL GASTRECTOMY IN THE TREATMENT OF BLEEDING VARICOSE VEINS IN BANTI'S SYNDROME\*

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OF THE VARIOUS OPERATIVE procedures that have been used for esophago-gastric hemorrhage in Banti's syndrome, splenectomy, porta-caval shunt and injection of the esophageal varices with sclerosing solutions are the only ones of much value.

Splenectomy<sup>1, 2</sup> has given its best results in the uncommon cases with blockage of the splenic vein. When extrahepatic obstruction of the portal vein is present, splenectomy, by removal of a large area of the portal bed, may ameliorate the hemorrhage for a variable length of time, but it usually recurs as the hypertension is built up again. Porto-caval shunt<sup>3, 4, 5</sup> introduced by Whipple and co-workers is the ideal treatment, since in addition to reducing the elevated pressure and tendency to hemorrhage of the gastro-esophageal varices, it relieves the passive congestion of all structures drained by the portal system. But in some cases of fibrous or cavernomatous transformation of the portal vein, it has been impossible to anastomose either the main trunk or one of its large tributaries with the inferior vena cava even when a vein graft was utilized. Also when anastomosis was possible, the communication has sometimes narrowed or closed. Previous splenectomy precludes splenorenal anastomosis. After successful anastomosis, there is still the possibility of hemorrhage from the already established gastro-esophageal varices.

In certain hands<sup>6, 7</sup> the injection of esophageal varices with a sclerosing agent has frequently controlled esophageal hemorrhage for worthwhile periods of time. Moersch<sup>8</sup> of the Mayo Clinic has recently made a follow-up study of 22 cases for periods of three or more years after injection. Twelve have had no more bleeding, four are living with continued hemorrhages, three are dead of hemorrhages, and four are dead of unknown or unrelated causes.

An additional measure to be considered when these techniques either have failed or for emergent or other reasons cannot be applied, is resection of the bleeding segment. This is especially true since the recent mortality for both transthoracic esophago-gastric resection<sup>9</sup> and total gastrectomy<sup>10, 11</sup> for carcinoma in experienced hands is under 15 per cent and after either operation at least a fair state of health may be maintained for an indefinite period. The first reported case of one-stage, transthoracic esophago-gastric resection, performed by Adams and Pheemister,<sup>12</sup> is alive and well nine years after operation and patients have lived for years after total gastrectomy with only mild anemia and slight impairment of nutrition.

Two patients with Banti's syndrome have been treated, one by total gastrectomy and one by transthoracic esophago-gastric resection. In each case

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\* Read before the American Surgical Association, March 25, 1947, Hot Springs, Va.

the hemorrhages began at an early age and persisted after splenectomy, the liver was normal and the general health was little impaired except by the bouts of bleeding

### CASE REPORTS

**Case 1**—C C, male, age 18 years, was admitted to the hospital 7-7-44 with the chief complaint of hemorrhages from the gastro-intestinal tract beginning at the age of six. Since the age of four his general health had been below par and he had had periodic attacks of malaise, weakness and fever. At the age of five an enlarged spleen was noted and since the age of six he had had repeated bouts of hematemesis and melena which were often associated with febrile attacks. At the age of ten he entered the Children's Memorial Hospital, Chicago, where he was found to have a markedly enlarged spleen and blood examination revealed R B C 395,000, Hb 70 per cent, platelets 6800, W B C 3000, Diff Polym 63, L 32, M 4, E 1, Ret 3 per cent, coag t 3 min, Bl t. 4 min.

Splenectomy was performed. The spleen weighed 325 Gm and microscopically showed the picture characteristic of Banti's disease. Following the splenectomy he continued to have bouts of hematemesis and melena and at the age of 16 they increased in severity. Eighteen months before admission, an esophagoscopic examination elsewhere revealed extensive varices of the lower and middle portions of the esophagus. Injections of the varices with a sclerosing solution were made on eleven occasions at that time, on nine occasions five months later, and on five occasions seven months after that. But two to four months after each set of injections, very severe bouts of bleeding occurred calling for numerous transfusions. The only change was that after starting the injections, the blood all passed by rectum, whereas before it has passed both by mouth and by rectum.

On admission, two months after the last hemorrhage, he felt well except for moderate weakness. Physical examination revealed essentially normal findings aside from an old left upper paramedian laparotomy scar. There were no paraumbilical varices or hemorrhoids. The liver was not palpable and the cephalin flocculation, colloidal gold and bromsulphalein liver function tests were normal. Blood examination showed R B C 5,100,000, W B C 8,900 and Hb 14 Gm per cent. On esophagoscopic examination the lining of the middle and lower esophagus was thickened from the previous injections and few varices were seen. Roentgenologically, when the Valsalva test was applied, the esophagus showed some irregularity of the barium shadow and the proximal stomach showed filling defects which were interpreted as due to varices. The stomach was manipulated under the fluoroscope and the patient soon presented symptoms of hemorrhage which became severe. Bleeding continued irregularly for 20 days, and necessitated 24 blood transfusions.

The diagnosis was made of bleeding gastric varices and a total gastrectomy decided upon. Severe bleeding started again on the early morning of the day for which the operation was scheduled. Rather than risk the chances of another severe bout of bleeding, an emergency laparotomy was performed. The stomach contained a large amount of blood and the coronary vein and branches to the lesser curvature were enlarged. There was blood in both small and large intestines and no sign of enlargements of the branches of the superior mesenteric vein. The liver was of normal appearance. Total gastrectomy, esophago-jejunostomy and jeuno-jejunostomy were performed. Bleeding continued during the operation and 3500 cc of partly clotted blood was found in the excised stomach. Thirty-one hundred cc of blood was transfused during and shortly after operation. The postoperative course was relatively uneventful.

**Pathology**—Externally the stomach looked normal aside from the moderately dilated veins on the lesser curvature. The gastric mucosa had normal folds and was of normal color except for a few petechiae. No ulcer or definite point of bleeding was found.

Microscopically, the outstanding feature in sections from all parts of the stomach

was the large size of submucosal veins and mucosal venules. Especially large, empty, submucosal veins were found near the lesser curvature, close to the cardia (Fig 1). Some of them had thin walls, with plaques which appeared to have been formed from organized mural thrombi. No fresh thrombi or open vessels were observed, here or



FIG 1—Case 1 Collapsed submucous gastric varices near the cardia ( $\times 9$ )

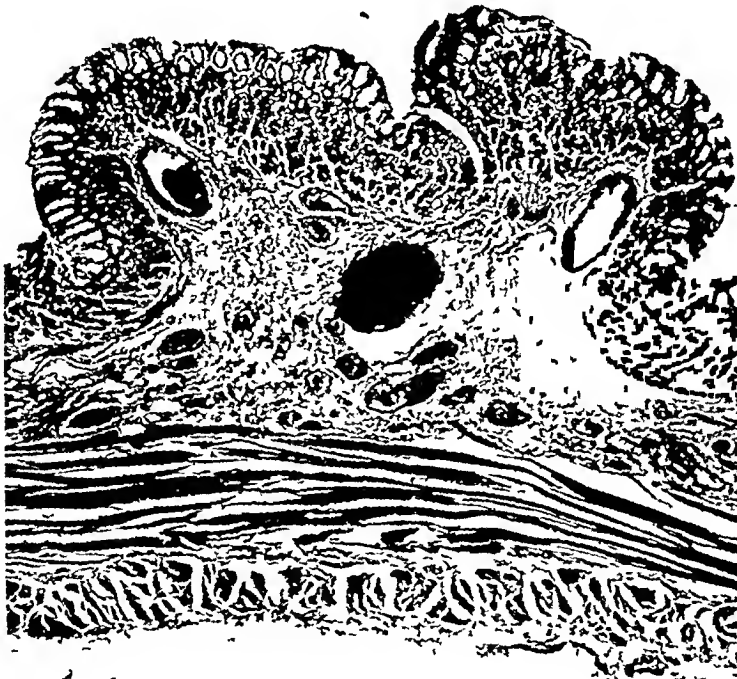


FIG 2—Case 1 Dilated veins in the wall of the fundus ( $\times 27$ )

elsewhere. The loose structure of the connective tissue adjoining the veins was probably an artifact. In the distended state the flat collapsed vein of Figure 1 must have caused the mucosa to bulge, and may have impinged on the dense fibrous tissue close to the muscular coats.

Many of the rugae contained numerous submucosal veins, sometimes as in the fundic



fold illustrated in Figure 2, stimulating an angioma. The two large veins in this fold protruded through the muscularis mucosae. Often connections could be traced between mucosal and submucosal veins. Such a channel in the mid-gastric region (Fig 3) drained the basal venous plexus of the mucous membrane, and the numerous venules and capillaries between the gastric glands. It was sometimes possible to trace serially one of the large straight venules from a channel communicating with a large submucosal vein almost



FIG 3—Case 1. Mucosal venocapillary network communicating with large submucosal gastric vein. Mid-gastric region ( $\times 125$ )

to the mucosal surface. At no point, however, was there a continuous demonstrable passage leading to the lumen. However, it is easily understood that bleeding might occur from minute surface erosions opening the tips of such vessels which would escape detection.

Even in the antrum and close to the pylorus venous distention and mucosal changes were evident, though nowhere so marked as near the cardia. Hemorrhage about a large pyloric vein as it passed through the muscle coats was probably the result of operative trauma. The largest external veins were close to the cardia. These coronary veins were not thrombosed, and were remarkable only because they were sclerotic, with walls thicker than those of the arteries they accompanied.

During the two and two-thirds years since operation, the patient has been in fairly good health aside from two bleeding spells, one moderate two years ago, and the other slight eight months ago. He has received injections of liver extract once a week and on 2-5-47, a blood examination revealed R B C 4,320,000, W B C 6900 and Hb 13.6 Gm per cent. Two years after operation, esophagoscopy revealed sclerosed bluish ridges in the lower esophagus but no definite varices were identified by needling and aspiration. This finding spoke against the reestablishment of important venous connections across the line of esophago-jejunal anastomosis. However, there was hematemesis at the time of the last bleeding, indicating that the blood came from esophageal varices.

**Case 2**—E. K., a female age 21 years, was last admitted three and two-thirds months ago because of melena and other symptoms of hemorrhage of five hours' duration. She first entered the hospital at the age of nine years with a history of occasional bouts of hematemesis and melena since the age of four, some of which had been severe and associated with febrile reactions. Two days previously she became ill with a fever and on admission the temperature was 39°C. The only other positive finding on physical examination was a moderately enlarged palpable spleen. The initial blood examination revealed R B C 4,960,000, Hb 96 per cent, W B C 12,050. Ten hours after admission bleeding started with hematemesis, and marked signs of blood loss and melena followed. Six days later she was afebrile, the bleeding had stopped and the blood examination revealed R B C 2,720,000, Hb 6.5 Gm per cent, W B C 4,700, coagulation time three minutes, bleeding time five minutes, platelets 260,000. Esophagoscopy revealed varices in the lower esophagus. A diagnosis was made of Banti's disease with bleeding esophageal varices.

Splenectomy was performed three weeks after admission when the patient had sufficiently recovered. The liver appeared to be essentially normal. The spleen weighed 167 Gm and was normal in contour. Microscopically, there were the changes of congestive splenomegaly with early stages of Banti's fibroadenoma. A hyaline thrombus was found in a small branch of the splenic vein near the hilus.

The postoperative course was uneventful. Blood examination six weeks after operation revealed R B C 4,370,000, Hb 74 per cent, W B C 9,150, platelets 828,000. Six months later the platelets were 215,000. At widely varying intervals, since the splenectomy the patient has had bleeding spells often associated with fever because of which she was repeatedly admitted for treatment. Otherwise she has been in good general health.

Five hours before the last admission, she developed weakness and faintness and soon passed a large amount of blood by rectum. Her condition grew worse and on admission she was in marked shock from hemorrhage. Blood examination revealed R B C 2,110,000, Hb 9 Gm and W B C 15,600, Prothrombin 95 per cent. Unconsciousness set in shortly before transfusion was started but she responded well to the continuous administration of 500 cc of plasma and 1500 cc of blood, followed by 2500 cc of blood in the course of the succeeding five days. The hemorrhage stopped and by the 8th day she was in good general condition. Roentgenography revealed varices in the lower esophagus (Fig. 4) which were verified by esophagoscopy.

In view of the nearly fatal outcome, the patient readily consented to operation. By a left thoracic approach through the bed of the resected 8th rib, the lower esophagus was exposed. No enlargement was noted in the veins about it. The diaphragm was opened and the liver found to be normal in appearance. The veins of the stomach were not remarkable although it was not easy to judge those of the lesser curvature. Resection of the lower three and one-half inches of the esophagus and upper two inches of the stomach followed by esophago-gastrostomy was performed. The postoperative course was uneventful, there has since been no return of bleeding and she is now in good general health.

**Pathology**—The mucosal surfaces of the resected segment are demonstrated in Figure 5. A few stringy brown clots adhered to the gastric mucosa which was grossly intact. Despite the previous oozing of much blood from the cut margins, tortuous submucosal



FIG 5—Case 2 Resected portions of esophagus and stomach, varices more extensive in esophagus than in stomach

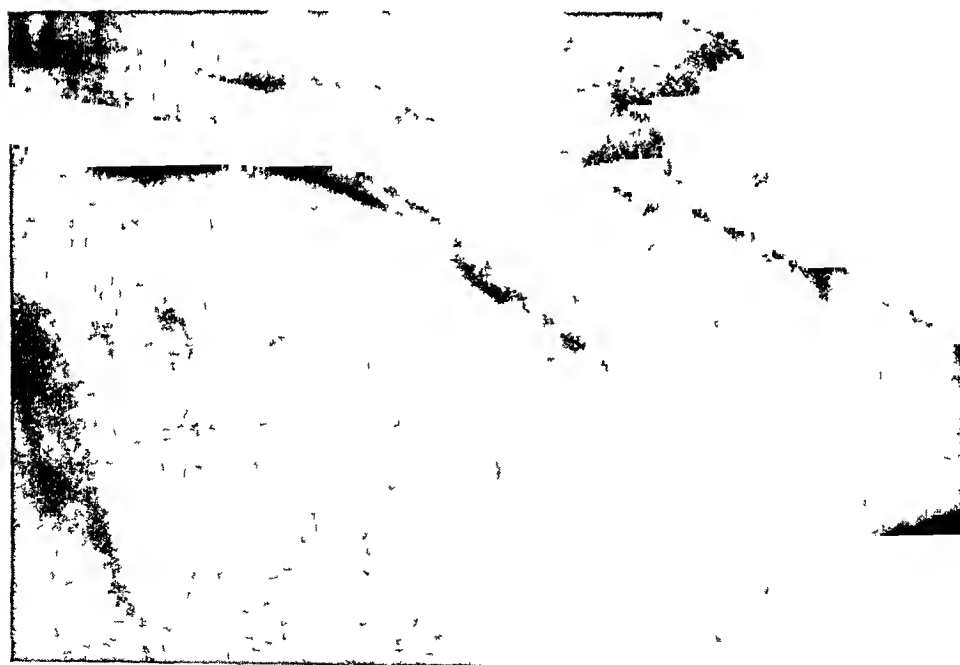


FIG 4—Case 2 Roentgenogram showing esophageal varices

veins were still conspicuous in both esophagus and stomach, but especially in the longitudinal folds of the esophagus. No gross defect in the esophageal epithelium could be demonstrated.

Microscopically, the largest esophageal veins were found to run in the submucosal tunic (Fig 6). They impinged on and deformed the muscularis mucosae, and occasionally broke its continuity. Numerous collapsed smaller veins ran in the thickened mucosa, where occasionally one reached the proportions of the submucosal veins. As in the large

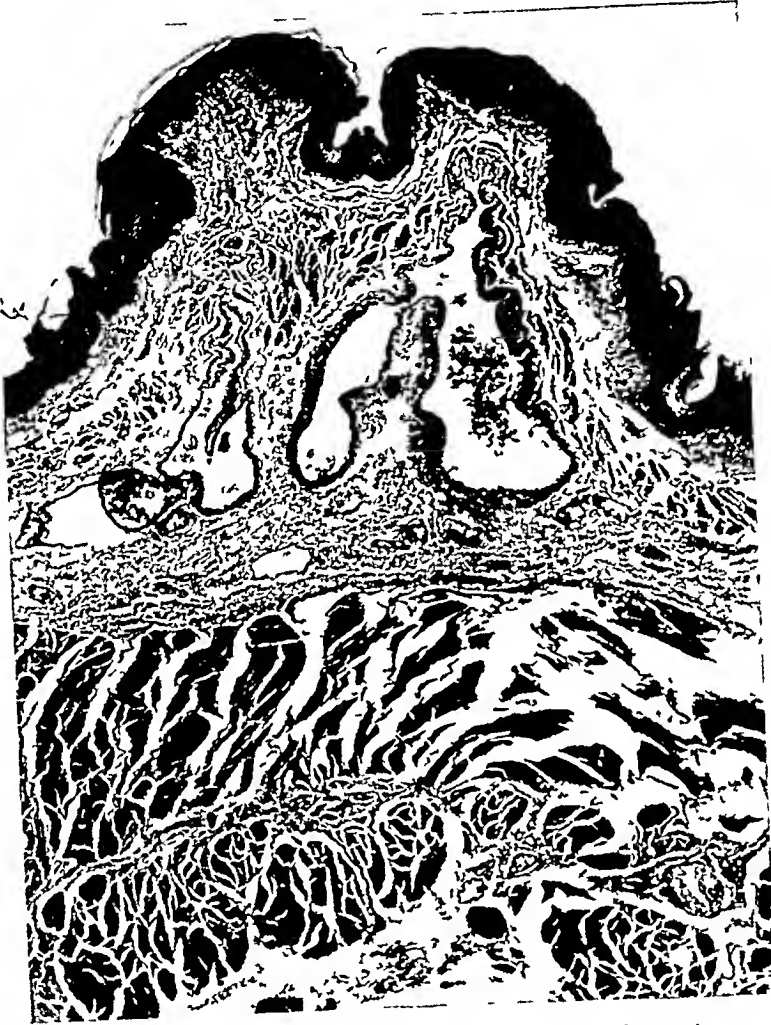


FIG 6—Case 2 Esophageal varices ( $\times 32$ )

veins of Figure 6, the walls of the venous channels were of variable thickness. The fibrous tissue of the inner tunics was condensed, and was particularly compact close to the epithelium covering the longitudinal folds. The epithelium was thick, and on the tops of projecting folds hyperkeratotic. On the tops of projecting folds no epithelial defects were found.

Microscopically, the changes in the gastric wall were in general similar to but much less pronounced than those in Case 1. The veins in the submucosa were considerably smaller than those in the esophagus but they were much more numerous than was apparent on gross inspection. The cross-section of a ruga close to the cardia, illustrated in Figure 7, demonstrates numerous wide veins. As in Figure 2 of Case 1, large veins impinged on the mucous membrane, and lay within or above the muscularis mucosae. Figure 8 illustrates in detail one of these veins lying in the basal portion of the mucosal venous plexus. The thickest part of its wall represents an organized mural thrombus. Its

large branch in the mucosa above is surrounded by dense fibrous tissue, representing an organized thrombotic vein. The artificially loose structure and distortion of the mucosa illustrated here was repeated in other sections which included large veins and wide venules. In some rugae the glandular pattern was even more distorted, resembling the changes illustrated in Figure 3 of Case 1. No erosions nor points of recent bleeding were identified.

No grossly visible defects to account for the recent hemorrhages were found in either resected specimen. The conclusion based on clinical facts that the stomach was the important source of bleeding prior to the gastrectomy in the first case was supported by

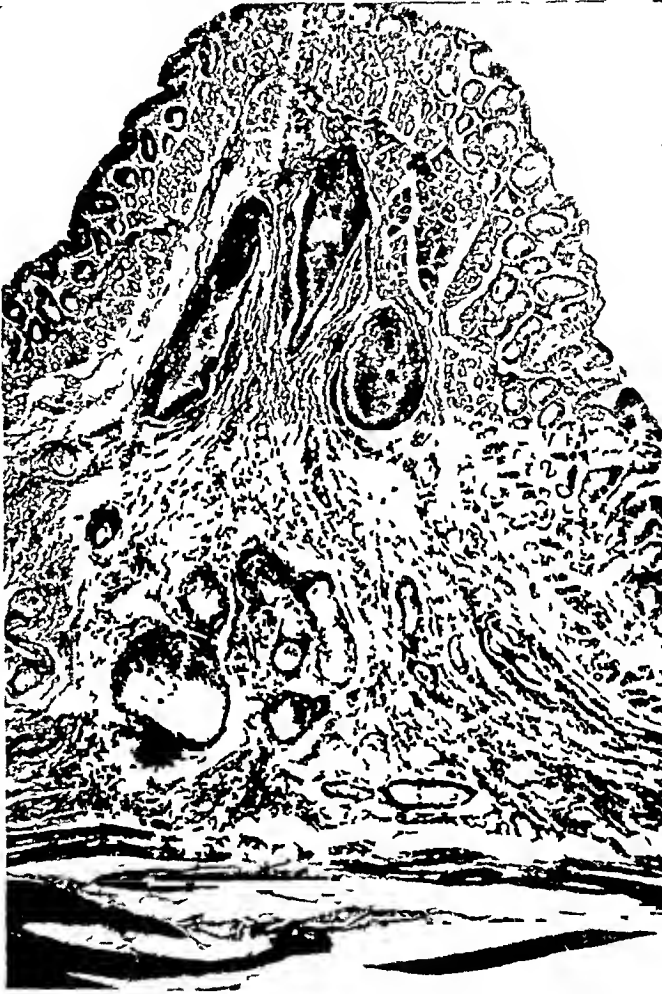


FIG 7—Case 2 Large veins in a gastric ruga (X 60)

histologic studies. Bleeding from the stomach as well as from the esophagus probably had occurred in the second case, judging from the presence of thrombosis in branches of the mucosa. Under some conditions, the gastric component of gastroesophageal varices may provide a greater danger of hemorrhage than the esophageal component.

#### DISCUSSION

The term "gastro-esophageal" fittingly characterizes the varices associated with chronic hypertension in the portal, gastric and splenic veins. Dilated gastric veins were demonstrated in both cases here reported. Especially in

Case 1, where sclerosing injections had obliterated many of the esophageal varices, gastric veins were everywhere enlarged, particularly so near the cardia. In Case 2, with patent esophageal varices, venous dilatation was similar but less marked. Clinical and anatomical evidence of recent severe gastric hemorrhage was present in Case 1, without grossly visible defects in



FIG 8—Case 2 Large vein lying internal to the gastric muscularis mucosae

the gastric mucous membranes. The fact that bleeding may occur without gross erosions explains the frequent lack of emphasis on gastric hemorrhage associated with gastroesophageal varices<sup>13, 14</sup>. The probable sources of the blood lost from the stomach without demonstrable lesion are numerous tiny ruptures through veno-capillary stomata, with the loss of too few epithelial cells to be appreciated grossly. In the average case of cirrhosis, or of Banti's syndrome, the esophageal varices are probably the source of most of the severe and sudden hemorrhages. However, these cases demonstrate how gastric bleeding may be added to esophageal bleeding, or as in Case 1, may replace it in importance.

The time has not arrived for a final evaluation of all of the various operative procedures for the control of hemorrhage in Banti's syndrome due to extrahepatic portal block. Resection of the bleeding segment like obliteration of the esophageal varices by injection, throws more load on the remaining routes of collateral circulation, but this may be justifiable because they either do not bleed at all or bleed infrequently, and if patients with extrahepatic portal block and portal hypertension especially the splenectomized ones, do not bleed to death, they may live indefinitely in good health except at the time of the bleeding bouts. Transthoracic esophagogastric resection gets rid of that portion of the varicose segment which is the usual seat of major hemorrhage, divides the vessels of the lesser curvature and of a variable part of the greater curvature, thereby reducing gastric blood supply and establishes more or less of a permanent barrier in the esophagogastric venous collaterals at the line of anastomosis. Total gastrectomy gets rid of the bleeding points when the hemorrhage is predominantly from the stomach and establishes a connection between the esophagus and jejunum which is free of varices.

Theoretically and from the meager information furnished by these two cases, resection would appear to be worthy of a trial when control of hemorrhage is impossible by means of splenectomy, porta-caval shunt and injections. Whether in threatening and emergent cases such as these two, the percentage of failures with porta-caval shunt and injections may be great enough to warrant the use of resection in advance of one or both of those procedures, remains to be determined. Splenectomy might be combined either with transthoracic esophagogastric resection, or in case of gastric bleeding, with total gastrectomy, if on exploration it is found impossible to perform a porta-caval shunt. Since wider resections than were practiced here are possible, they might be called for in selected cases.

#### SUMMARY

A patient with Banti's syndrome and a normal liver had frequent severe hemorrhages from gastric varices after splenectomy and extensive obliteration of esophageal varices by injections had been carried out. Total gastrectomy was performed two years and eight months ago, since which time there have been only two bleeding spells from remnants of the esophageal varices, one moderate and the other slight.

A second patient with Banti's syndrome and a normal liver was subject to severe hemorrhages which continued after splenectomy. Transthoracic esophagogastric resection was performed and varices were found in the resected segment, greater in the esophagus than in the stomach. There was no further bleeding three and one-half months after operation.

The importance of gastric varices as a source of hemorrhage is discussed.

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DISCUSSION—DR ALFRED BLALOCK, Baltimore, Md Approximately two years ago I operated upon a 39-year-old woman who had bleeding esophageal varices with the intention of carrying out a procedure such as Doctor Phemister and Doctor Humphreys have described On opening the left lower pleural cavity many varices could be seen on the outside of the esophagus Two large plexuses of such vessels were removed (lantern slide showing dilated veins) We performed this operation rather than that of removal of the lower part of the esophagus because it appeared to be a less dangerous one However, the bleeding continued and I wished subsequently that I had carried out the procedure described by Doctor Phemister

Fortunately this patient had not had her spleen removed and in that respect she presented a problem somewhat different from that of the patients described by Doctor Phemister Since the bleeding continued, we decided to perform a renal splenic vein anastomosis as developed and popularized by Dr Arthur Blakemore and Dr Allen Whipple

(Motion picture showing renal splenic anastomosis) The incision was performed through a left transverse abdominal incision Other methods of approach have been recommended For example, Doctor Linton of Boston uses a left transpleural approach The spleen was used, exercising great care not to injure the splenic vein The kidney was delivered into the incision The renal artery was occluded temporarily The renal vein was occluded proximally and distally with rubber shod clamps and a transverse opening was made into the vein between the points of occlusion An end-to-side anastomosis was then performed between the proximal end of the splenic vein and the side of the left renal vein The intima was approximated and everted by the use of 00000 silk on an atraumatic needle By the use of the end-to-side anastomosis, it is not necessary to sacrifice the kidney Furthermore, the experimental observations of Dr T N P Johns



and myself indicate that an end-to-side anastomosis is more apt to remain patent than is an end-to-end anastomosis in which the kidney is removed. It seems likely that the blood returning from the kidney serves to maintain patency of the anastomosis. A better procedure is that recommended by Doctor Blakemore, in which one only partly occludes the renal vein during the time that the anastomosis is being performed. This was not possible in the present case because the renal vein was not very large.

The present patient has had no further bleeding since the operation, but the interval has been only a couple of months. However, the results in other cases upon whom Doctor Blakemore, Doctor Linton, I and others have operated with a longer time follow-up are encouraging.

Nevertheless, I must agree with Doctor Phemister that patients with bleeding esophageal and gastric varices present exceedingly difficult problems and it is quite likely that the best means of treating them has not yet been evolved. I am very much impressed by the results reported by Doctor Phemister and I think that this method will find further useful application in the treatment of bleeding varices, and particularly so in the case of those patients who have had a previous splenectomy.

DR OWEN H. WANGENSTEIN, Minneapolis, Minn. Doctor Phemister stressed the hydrostatic factor as the important one in bleeding from esophageal varices. There is another item which, I believe, may be equally as important, viz., the acid-peptic digestive factor.

Bleeding from the mucosa of the lower esophagus or stomach in the presence of portal hypertension, whether occasioned by portal cirrhosis or Banti's disease, appears to be due in part to the circumstance that erosions in these areas are readily produced in the presence of portal hypertension. This evidence has been published elsewhere (Canadian Med Assoc J 53, 309, 1945) and here it need only be said that portal hypertension definitely abets the ulcer diathesis. In our laboratory, histamine implanted in beeswax has proved a useful tool in exploring factors which are believed to abet the ulcer diathesis as well as in assaying the protective merits of an operation against ulcer. Whereas, a 75 per cent gastric resection performed with a short afferent duodenojejunal loop will protect dogs regularly against the histamine-in-beeswax provoked ulcer, a 90 per cent resection will not protect regularly when a simultaneous portal hypertension has been brought about (Proc Soc Exper Biol & Med 59, 234, 1945).

The late Professor Eppinger pointed out in his monograph on liver disease that approximately 20 per cent of patients with cirrhosis die of hemorrhage. Deaths from hemorrhage and ascites in portal hypertension are owing essentially to mechanical causes—the increased venous pressure, and may precede actual hepatic insufficiency by a long interval. All operative procedures directed at correcting hemorrhage in progressive hepatic cirrhosis are essentially palliative in nature, for we do not know how to arrest failure of hepatic functions. Yet, life may be prolonged through operative procedures which lessen the tendency to hemorrhage. In the Blakemore procedure this end is achieved by diverting the blood from the portal system to one of the systemic veins. In cirrhosis such a procedure may not improve liver function and in thrombophlebitis of the portal and splenic veins (Banti's disease) the thrombus may extend and compromise the return of blood from the small intestine.

In performing total gastrectomy for bleeding esophageal varices, in addition to getting rid of the acid-peptic digestive factor, Doctor Phemister did one other important thing, he separated the esophagus completely from the higher venous pressure of the portal circulation. In the 90 to 98 per cent gastric resection which I have employed for esophageal or gastric hemorrhage occasioned by portal hypertension, this latter feature of total gastrectomy is absent, in that one or two vasa breviae still connect the submucosal lakes of the lower esophagus to the portal circulation. I am inclined to believe that a 95 to 98 per cent gastric resection or a total gastrectomy are physiologically sound in the management of esophageal varices even though they do not approach the problem as

directly as does esophagogastric resection. Moreover, patients with bleeding from the upper reaches of the alimentary tract who have hepatic cirrhosis or Banti's syndrome appear to have generous amounts of free hydrochloric acid in their gastric juice. When on exploration, the liver appears normal as it usually does in Banti's disease, the management of the venous pressure in one of the tributaries of the portal vein is important. In thrombophlebitis of the portal vein, the venous pressure will be up, whereas in bleeding from a silent, nonpalpable gastric erosion, the venous pressure will be normal. For the latter type of case, the conventional 75 per cent gastric resection is adequate, for the portal hypertension, a 95 per cent resection should be done.

Of the three patients reported by me in 1945 who underwent extensive gastric resection for bleeding from esophageal varices, two are still alive and well. Neither has had recurrent hemorrhage. I had done earlier excisions of the spleen in both with recurrent hemorrhage. The first patient, a man who underwent ligation of the veins to the lower esophagus elsewhere, prior to submitting to a 90 per cent gastric resection at my hands, died somewhat less than a year later from complete obliteration of the portal vein. Moreover, there had been some melena prior to death. But as was related above, a 90 per cent gastric resection does not protect regularly against the histamine-provoked ulcer in the dog in the presence of portal hypertension. A few months after the extensive gastric resection, I also excised this man's right lung for carcinoma. Of the two surviving patients, one is a child with nodular hepatic cirrhosis for whom a 98 per cent gastric excision was done for repeated hemorrhages persisting ten months after splenectomy. This boy is now almost six years old and has had no recurrent hemorrhages two years after the gastric resection. The other is a young woman in her thirties with Banti's syndrome of thrombophlebitis of the portal and splenic veins. Her spleen was excised by me seven years previously with persistence of hemorrhage. There has been no recurrence of hemorrhage since the 95 per cent gastric resection done almost two years ago.

DR J. DEJ. PEMBERTON, Rochester, Minn. For many years I have been interested in the problem presented by Doctor Phemister, that is, the control of bleeding from esophageal and gastric varices in cases of Banti's syndrome.

In the past at the Mayo Clinic we have relied on two measures to check such bleeding, both of which are designed to reduce the hypertension of the portal circulation, namely (1) removal of the actively congested spleen in order to diminish the volume of blood entering the portal system and, (2) performance of omentopexy in order to promote the establishment of collateral circulation between the portal and caval systems. Results of such treatment as regards prevention of recurrent bleeding may be summarized briefly. Of the 173 patients who had hemorrhage before operation, 93, or 54 per cent, have had recurrent bleeding after operation, but of the 99 patients who had no gross bleeding before operation, 15 per cent have had subsequent bleeding. These clinical data would tend to support the belief that if splenectomy were performed early in the course of the disease before the development of esophageal and gastric varices, bleeding could be prevented in a large percentage of cases of Banti's syndrome.

After the demonstration by Crafoord and Frenckner in 1939 that esophageal varices could be obliterated safely by the injection of sclerosing solution, my colleague, Dr. Herman Moersch, has employed this method of treatment in a series of patients who had recurrent bleeding after splenectomy. Doctor Moersch has kindly furnished me with a brief summary of the results of injection of the esophageal varices in 22 cases in which patients were treated up to three years ago. Twelve patients were completely relieved of their bleeding. These patients have been followed up for from four to six years. Apparently in all these cases the varices were confined to the esophagus. The results in the remaining ten cases were unsatisfactory. In all ten, varices were demonstrable in the cardiac end of the stomach, as well as in the esophagus. The results are as follows. Three patients died of further bleeding, one patient died, cause unknown, one patient died of cerebral hemorrhage, one patient died of hepatic insufficiency, and four patients are alive but have had further bleeding.

Doctor Moersch feels, therefore, that the injection is an effective method of preventing bleeding in those cases in which the varices are limited to the esophagus, but that it is of little or no value in those cases in which the varices extend into the cardiac end of the stomach. It is for patients in this latter group of cases that further measures are needed in order to prevent bleeding, and I believe that Doctor Phemister's procedure is a logical approach to the problem. It may appear too radical, but I am convinced that any procedure, however formidable, which offers any reasonable hope for these patients is definitely warranted. I want to congratulate Doctor Phemister.

DR ARTHUR H BLAKEMORE, New York City. On the basis that in cases having portal hypertension, the most frequent sites of hemorrhage are from gastric veins and esophageal varices, Doctor Phemister and his associate have removed the stomach and lower esophagus in two cases.

Such a procedure obviously deals effectively with any varicosities existing within the limits of the resection, but fails to correct the underlying cause. In re-establishing the continuity of the alimentary tract, Doctor Phemister has anastomosed the esophagus to the jejunum. The venous drainage from the esophagus is into the caval system via the azygos veins. The venous drainage of the jejunum is into the portal system. At the site of the anastomosis, branches of the caval system anastomose with branches of the portal system and, in the presence of portal hypertension, the subsequent development of varices is inevitable.

In the past, radical excisions of the anastomosing system of portal and caval branches has failed to relieve hemorrhage in the presence of portal hypertension.

DR DALLAS B PHEMISTER (closing). It should be emphasized that gastric or esophageal hemorrhage in Banti's Syndrome is usually the result of rupture of varices that lie immediately beneath the mucosa or even extend out into its substance, and that it is not associated with the deeper and more extensive ulceration mentioned by Doctor Wangenstein, which is met with in the ulcer patient or in ulcers produced experimentally in animals by histamine implantation.

Doctor Blakemore has pointed out that gastro-esophageal resection throws an extra load on the other points of collateral circulation. This is true, but they rarely ever bleed. For example, I have not seen bleeding hemorrhoids in a patient with Banti's Syndrome. Consequently, resection may be justified.

# ACUTE CHOLECYSTITIS FOLLOWING THE SURGICAL TREATMENT OF UNRELATED DISEASE\*

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ACUTE CHOLECYSTITIS following surgical operations other than on the biliary tract has attracted the occasional attention of surgeons for some time Vest<sup>1</sup> reported a case from the Union Memorial Hospital in Baltimore of a 22-year-old woman who was operated on for subacute appendicitis. Palpation of the gallbladder at operation was reported normal. She made an uneventful recovery and was discharged a week after operation. Three days later she was seized with sudden intense pain in the upper abdomen associated with marked spasm and tenderness in the gallbladder region. A gallbladder containing large amounts of black bile and a single mulberry stone was removed after readmission to the hospital. Fisher<sup>2</sup> reported another case from Baltimore of a 19-year-old football player who was operated on for open reduction of the scaphoid. Two days later he developed manifestations of acute cholecystitis with a white count of 17,200. At operation a gangrenous gallbladder was removed and the patient made an uneventful recovery. One of the earliest cases in the literature was reported by Duncan<sup>3</sup> in 1844. The patient was a woman with a strangulated hernia of 24 hours' duration and general symptoms of intestinal obstruction. The hernia was easily reduced but the symptoms became more severe and suggestive of peritonitis. Death occurred in 48 hours. Postmortem showed the under-surface of the gallbladder to be gangrenous, it had perforated, resulting in bile peritonitis. No stones were found. Another instance was reported by Kocher<sup>4</sup> of a 51-year-old woman who developed acute symptoms of cholecystitis eight days after repair of a ventral hernia. At operation a gangrenous gallbladder was found.

Several years ago I saw at autopsy a patient who had died because of a generalized peritonitis secondary to an acute gangrenous cholecystitis with a free perforation into the peritoneal cavity. The patient was a 60-year-old male who had been operated upon for repair of a large sliding hernia that contained much of the sigmoid colon. He was obese, weighing 74.2 kilos. The operation was done without difficulty under spinal anesthesia. Because of the dissection required to liberate the incarcerated bowel, the patient after operation was maintained on clear liquids by mouth and infusions for six days. The diet was then increased and on the seventh postoperative day he complained of abdominal pain that was first generalized and then became most marked on the right side. This was accompanied by an elevation of temperature to 38° C, an increase in the pulse rate to 100, and marked abdominal distention. The latter was only partially relieved by enemas. Nausea and vomiting were marked on the 9th postoperative day and a flat plate revealed

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\* Read before the American Surgical Association, March 25, 1947, Hot Springs, Va

marked large bowel distention. Because of these symptoms and findings, a laparotomy was done ten days after repair of the hernia and particular attention was directed to the left colon which had been incarcerated in the large hernia. The fluid in the abdomen was blood-tinged and the lower bowel was distended but otherwise not unusual. The region of the gallbladder was not examined, although a colostomy of the transverse colon was done in an effort to relieve the bowel distention. Five days later the patient died. The gangrenous gallbladder containing stones had perforated into the peritoneal cavity, resulting in a generalized peritonitis, the cause of death.

Over a period of 14 years (from September 1, 1932, to September 1, 1946), at the New York Hospital, a total of 555 patients have been operated upon for acute cholecystitis. This phase of gallbladder disease, we feel, is well treated by surgery and for those patients under 50 years of age the operative mortality has been low, there having been four deaths, a mortality rate of 1.08 per cent in a group of 368 patients. The mortality rate was much higher in the 187 patients over 50 years of age, there were 11 deaths, a mortality rate of 6.1 per cent. During this same period over 2,000 patients were operated upon for non-malignant disease of the biliary tract.

TABLE I  
ACUTE CHOLECYSTITIS—NEW YORK HOSPITAL  
*September 1 1932 to September 1 1946*

Total cases	555
Deaths	15
Mortality per cent	2.7
Operative Procedures	
Cholecystectomy	485
Cholecystostomy	70*
Common duct exploration	44
* 12.6% of total operations	

Cholecystostomy was performed in 70 instances and was followed by six deaths. This procedure is clearly indicated under certain circumstances, as when the patient is too ill to withstand cholecystectomy or when cholecystectomy presents too great difficulties. For the extremely debilitated patient or for the very ill, we doubt if there are any contraindications for cholecystostomy because it may be done under local anesthesia, disturbing the patient very little, and at the same time the simple procedure may be a life-saving one. The decompression of the biliary tract averts catastrophe by preventing progressive liver damage if complete biliary obstruction is present.

TABLE II  
ACUTE CHOLECYSTITIS—NEW YORK HOSPITAL  
*September 1 1932 to September 1 1946*  
Patients fifty years of age or over

Total cases	187
Deaths	11
Mortality per cent	6.1
Operative Procedures	
Cholecystectomy	150
Cholecystostomy	37*
Common duct exploration	24
* 19% of total operations	

In the series of 555 patients treated surgically, 187 were 50 years of age or over. There were 11 deaths, a mortality rate of 6.1 per cent. One hundred and fifty were subjected to cholecystectomy. Thirty-seven, or 19 per cent of the 187, were treated by cholecystostomy. Twenty-four, had in addition to these operations, exploration of the common duct. The mortality rate of 6.1 per cent of these patients who were 50 years of age and over indicates the definite greater risk associated with them than those of less than 50 years of age with a mortality rate of 1.08 per cent.

TABLE III  
ACUTE CHOLECYSTITIS—NEW YORK HOSPITAL  
*September 1, 1932 to September 1, 1946*  
Patients under fifty years of age

Total cases	368
Deaths	4
Mortality per cent	1.08
Operative Procedures	
Cholecystectomy	334
Cholecystostomy	33*
Common duct exploration	26
* 9% of total operations	

The remaining 368 of the 555 patients were under 50 years of age. There were four deaths, a mortality rate of 1.08 per cent. Three hundred and thirty-four, or 90.8 per cent, were subjected to cholecystectomy, and 33, or 8.9 per cent, were treated by cholecystostomy. Only 26, or 7.1 per cent, had in addition to one of the above procedures, exploration of the common duct. This is a far more favorable outcome than our experience with the group of patients who were 50 years and over.

During this period of 14 years I have observed 17 patients who developed acute cholecystitis following a surgical procedure unrelated to the biliary tract. They are as follows:

Diagnosis	Number Cases	Age of Patients
Hernia	4	60-62-60-58
Acute appendicitis	2	67-32
Hemorrhoids	2	60-58
Hydrocele	1	63
Fissure in ano	1	54
Ovarian cyst	1	29
Abscess of leg	1	67
Nasal packing for epistaxis	1	41
Bladder stones, hypertrophy of prostate	1	64
Tumor of salivary gland	1	63
Hypertrophy of the prostate	1	54
Carcinoma of the rectum	1	49
Total	17	

Five of these patients were observed during the last part of 1945 and 1946. Their case summaries are presented as illustrative of the common course of events.

**Case 1 C S—#438487** This 67-year-old white male was admitted to the hospital because of a cellulitis superimposed upon dependent edema of the lower extremities secondary to cardiac disease. The cellulitis had followed a severe sunburn sustained in Florida. He was admitted to the hospital, placed at rest in bed, and digitalized. During this period he developed a subcutaneous abscess that was incised and drained under local anesthesia. He received morphine and codeine for discomfort and because of his cardiac condition was placed on limited intake by mouth. He received penicillin for his infection. Eight days after admission and two days after incision and drainage of the abscess, he suddenly developed pain in the right side of his abdomen associated with nausea and vomiting. There was no history of any similar previous episodes. His temperature within a few hours was  $38.4^{\circ}\text{C}$  and his white count rose to 22,300. The entire right side of the abdomen was held so rigid that no masses could be palpated. A diagnosis of probable acute cholecystitis was made and under local anesthesia a cholecystostomy was done. There was bile-stained fluid free in the peritoneal cavity, the gallbladder was tense and acutely inflamed. It contained white bile and bile-stained material but no stones. The patient's postoperative course was satisfactory. Because of his cardiac condition he was discharged from the hospital and died some weeks thereafter of cardiac disease.

**Case 2 S G—#461002** A 32-year-old male was operated upon for acute suppurative appendicitis with gangrene, having had symptoms for about three days prior to operation. Following the appendectomy the patient received nothing by mouth for several days because of peritonitis, morphine was given for pain. He had glucose infusions up to 3,000 cc per day. He was a somewhat apprehensive individual who was very slow in resuming a normal intake by mouth. Solid food was first taken on the 9th postoperative day, the next day he complained of pain in the right upper quadrant which gradually increased in severity. He became nauseated and vomited, and associated with this was an elevation of temperature to  $37.8^{\circ}\text{C}$  and of the white count to 24,000. At operation a large, acutely inflamed gallbladder containing 50–60 stones was removed. His postoperative course was entirely satisfactory and he was discharged two weeks later. It is probable that the prolonged period of fasting and a moderate amount of drug therapy may have precipitated this acute attack.

**Case 3 C R—#446343** A 62-year-old man was admitted to the hospital for repair of an indirect inguinal hernia. In the course of a check-up cholecystograms were taken, revealing stones. The patient was operated upon for repair of the hernia under local anesthesia, having been given preoperative morphine, and clear fluids were given immediately after operation. He received morphine on the first postoperative day and codeine on the second, and he was then placed on a soft diet. On the third day he complained of severe pain in the right upper quadrant following the taking of a few bites of creamed shrimp. Within a few hours there was a palpable mass in the right upper quadrant which was believed to be the gallbladder. His white count was 12,000 and his temperature rose to  $38.4^{\circ}\text{C}$ . He was nauseated and vomited. A diagnosis of acute cholecystitis was made and operation recommended but refused by the patient. The acute episode gradually subsided over a period of three days and the patient was discharged from the hospital to return four months later when a gallbladder containing many stones was removed.

**Case 4 F C—#403668** A 41-year-old hotel executive was admitted to the hospital because of epistaxis which was severe and persistent. His past history was significant. Eight years before he had had acute cholecystitis, and a cholecystostomy was done and stones removed. Six years later because of indigestion he had had cholecystograms done which revealed a poorly functioning gallbladder containing stones. For years he had taken several cocktails and highballs each day. His prothrombin time was prolonged but became normal following the administration of vitamin K. Upon admission to the hospital he was given transfusions. Repeated packing of the left nostril was necessary.

and during this period the patient received morphine for pain and discomfort. Fluids were taken with difficulty and he received infusions, he took no food. He was running an elevated temperature of  $39.8^{\circ}\text{C}$  which gradually subsided over the first five days of hospitalization, at the end of which time he was greatly improved. His temperature was almost normal and he received solid food for the first time on the 5th day after admission. Shortly thereafter the patient had severe right upper quadrant pain radiating around the right costal margin. He was nauseated but did not vomit. Within a few hours the entire abdomen had become rigid to examination, the pulse was elevated to 120, the temperature to  $39.4^{\circ}\text{C}$ , and the white count to 13,000. It was the impression of the author that the patient had a perforation of the gallbladder associated with acute cholecystitis. He was subjected to immediate operation but because of his poor general condition only a cholecystostomy was done for acute gangrenous cholecystitis with a perforation through which bile was escaping. There was a single stone which was removed. He was discharged from the hospital 22 days later. Four months thereafter he was readmitted and a cholecystectomy was done.

**Case 5 P H—#455952** A 64-year-old male was admitted to the hospital because of a bladder stone and hypertrophy of the prostate. The patient had in addition to his urinary symptoms some indigestion, and prior to operation a cholecystogram was taken which revealed stones. Seven days after admission a suprapubic cystolithotomy and suprapubic prostatectomy were performed under spinal anesthesia. He received pre-operative morphine and also morphine after operation, as well as parenteral fluids. During the following six days the patient was without appetite and took only clear fluids. On the 7th postoperative day he began to take his first solid food. The following day he complained of pain in the right upper quadrant and was nauseated but did not vomit. Over a period of 12 hours there developed a mass in the right upper quadrant and generalized muscular resistance of the right rectus. His temperature rose to  $38.8^{\circ}\text{C}$  and the white count was 14,200. The patient was operated on and an acutely inflamed, distended gallbladder was found which contained a large stone in the ampullary region. Because the patient had at the time of this operation an upper respiratory infection as well as some elevation of his urinary nitrogen, the operation was performed under local anesthesia and only a cholecystostomy was done. Following this procedure he made an uneventful recovery and was discharged from the hospital on the 25th postoperative day. He is to return for cholecystectomy.

Because of the controversy commonly associated with the early surgical treatment of acute cholecystitis, we have been constantly reviewing our experience in an attempt to evaluate properly our policy. Our aim has been to interrupt biliary disease early by surgical interference. Acute cholecystitis is but a phase of biliary tract disease. It is an important phase, however, because in it certain complications may arise which are associated with a high mortality rate. And it has been reported again and again in the literature that these complications and their accompanying mortality account for a very definite proportion of the deaths that result from operations upon the gallbladder and bile ducts. In a paper entitled "The Factors Leading to Death in Operations Upon the Gallbladder and Bile Ducts," Heuer<sup>5</sup> in 1934 reported that 20 authors up to that time had recorded 502 instances of perforation of the gallbladder. Only eight of these recorded their mortality figures, however, these ranged from 33.3 to 100 per cent. In a review of the literature from 1934 to 1946 I have found reports of 25 authors who have recorded an additional 457 cases. Twenty-two of the 25 authors have given their mortality figures and these range from 5.8 per cent to 75 per cent.



TABLE IV  
GALLBLADDER PERFORATIONS FROM THE LITERATURE—DEATHS AND MORTALITY  
Heuer—1934

Author and Reference	Number	Number	Mortality
	Cases	Deaths	(Per Cent)
Blalock A Bull Johns Hopkins Hosp 35 391 1924	21	?	
Smith M Tr Am S A 51 287 1933	24	?	
Johnson South M J, 19 889, 1926	9	9	100 0
Judd Parker Ann Surg 84 419 1926	2	?	
Siegmund Deutsches Arch f Chr 230 359 1924	8	5	62 5
Heuer, G West Virginia M J 26 1 1930	18	?	
Danzia S Clin North America 6 1397 1926	1	1	100 0
Stanton Am J Surg 8 1026 1930	32	32	100 0
Santee Ann Surg 93 1156 1931	5	3	60 0
Alexander Ann Surg 86 765 1927	20	?	
Mitchell Ann Surg 88 200 1928	16	?	
McWilliams Ann Surg 55 235 1912	6	2	33 3
McWilliams Ann Surg, 55 235 cites	108	52	48 0
Gosset Deplas J de chir 25 259 1925	111	?	
Darner Cullen Surg Gynec. & Obst 37 579 1923	3	2	66 6
Zinninger Ann Surg 96 406 1931	16	?	
Miller Ann Surg 92 644 1930	8	?	
Graham Ann Surg 93 1152 1931	7	?	
Judd Phillips Tr Am S A 51 292 1933	68	?	
Mentzer Surg Gynec & Obst 55 709 1932	19	?	
Total	502		

TABLE V  
PERFORATION OF THE GALLBLADDER—ADDITIONAL CASES FROM THE LITERATURE  
Glenn—1947

Author and Reference	Number	Number	Mortality
	Cases	Deaths	(Per Cent)
Cowley & Hawkins Surg Gynec & Obst 77 661 1943	25	4	24 0
Edwards & Goerig Ann Surg 113 824 1941	18	3	16 6
Stone & Douglas Am J Surg 45 301 1939	17	1	5 8
Eliason & McLaughlin Ann Surg 99 914 1934	9	1	11 0
Niemeyer O Ann Surg 99 922 1934	8	0	0
Sanders R Surgerv 1 949 1937	46	8	17 4
Noble T Am J Surg 38 259 1937	9	3	33 3
Bachhuber & Deeb Am J Surg 67 40 1945	22	3	13 6
Johnston & Ostendorph Arch Surg 53 1 1946	3	0	0
Heyd C G Ann Surg 101 797 1935	6	1	16 0
D Abreu A. Brit M J 2 1156 1936	3	2	66 6
Hotz R Am J Surg 44 706 1939	53	19	35 8
Atlee J & Atlee J Jr Pennsylvania M J 44 731 1941	15	3	20 0
Schaeffer R Pennsylvania M J 45 566 1942	20	8	40 0
Graham & Hoefle Ann Surg 108 874 1938	4	3	75 0
Blain & Harkins Surgery 21 110 1947	9	5	55 0
Blumberg N & Zisserman L Am J Surg 70 38 1945	21	7	33 3
Root & Priestley Am J Surg 61 38 1943	22	8 ?	
Stout & Hibbard Surgery 13 734 1943	6	4	66 6
Eliason & Stevens Surg Gynec & Obst 65 79 1937	17	0	0
Wallace & Allen Arch Surg 43 762 1941	64	11	17 2
Wesson H Proc Staff Meet Mayo Clin 12 500 1943	16	0	0
Taylor F Surg Gynec & Obst 63 298 1936	15	3 ?	
Touroff A Ann Surg 99 900 1934	4	?	
Glenn & Moore Arch Surg 44 (677-686) 1942	25	4	16 0
Total	447		

The genesis of acute cholecystitis following unrelated surgical operations may be accounted for as follows The patient for a certain number of hours

before operation receives nothing by mouth, he then receives preoperative medication of morphine and atropine. It is believed that the flow of bile from the liver into the gallbladder is almost constant—the preoperative medication does not alter this. The bile is concentrated in the gallbladder. The operation then takes place, and the flow of bile under anesthesia may be reduced, but the operation is a matter of one to a few hours. Then the flow of bile into the gallbladder begins again. There is further concentration of bile in the gallbladder until some stimulus in the stomach or duodenum results in its emptying. At first the patient usually takes water, then clear liquids, full liquids and then a soft diet. Upon ingestion of a soft diet there may be, for the first time, since water and food were withheld before operation, an all-out attempt on the part of the gallbladder to empty its viscid and concentrated bile into the common duct and thence into the duodenum. If a stone or stones block the escape of the concentrated bile from the gallbladder then the mechanism for obstructive cholecystitis obtains and an acute episode in the cycle of gallbladder disease may result. However, there are instances of acute cholecystitis in our experience without stones.

The pathology of the gallbladder in the patient who develops acute cholecystitis following a surgical procedure is indistinguishable from that observed in patients commonly encountered. In cholelithiasis the degree of ischemia or edema would appear to depend upon the location and relation of the cystic vein and cystic artery to the segment of the cystic duct or ampulla, within which is lodged the stone. The gallbladder which has had many previous episodes of inflammatory reaction is more scarred and therefore does not become distended and enlarged to the extent that the more normal gallbladder does. Likewise the thickness of the gallbladder wall is dependent upon the amount of edema that may be the result of obstruction to the venous return and the nature and extent of the bacterial infection within the gallbladder wall. Certain types of infection, of short or long duration, tend to produce a great deal of reaction with the result that the thickness of the gallbladder wall is several times that of the normal organ. The thickness of the wall might determine to some degree the readiness with which perforation would take place, providing the type of infection were equal in the two. The rapidity with which gangrene develops and is followed by perforation is dependent upon the interference of the blood supply, the rapidity with which the infection takes place, and the virulence of the organism and its capacity to cause necrosis.

We would not imply that free perforation is to be anticipated in the majority of patients with acute cholecystitis. The omentum and its tendency to become attached to the inflamed gallbladder wall constitutes a normal protective mechanism, and it is probable that this comes into effect in the majority of patients. If the area of gangrene in the gallbladder wall is limited to the fundus then attachment of the omentum may block the free escape of bile into the peritoneal cavity. If, however, the entire organ is involved, then it is probable that the omentum will be unable to protect the peritoneal cavity. Where there has been a free escape of bile into the abdominal cavity, there is

usually an absence of any pretext of adhesions between the gallbladder wall and the omentum. Whether or not this is due to the action of the bile or whether there is some other process with which we are not familiar that prevents it fulfilling its normal function is not known. In late bile peritonitis the omentum as a rule seems to be contracted and much smaller, and assumes the normal position down over the mid-portion of the abdomen rather than traveling to the source of the bile leakage.

In discussion of the treatment of acute cholecystitis with those who favor nonoperative treatment, we are often confronted with the statement that perforation of the acute gallbladder rarely, if ever, occurs. Our experience at the New York Hospital and that reported by other clinics suggest that it is much more common than is generally accepted.

Johnstone and Ostendorph<sup>6</sup> found on review of 12,000 consecutive routine autopsies done at the Los Angeles Hospital from 1936 to 1942 a total of 32 instances of perforation of the gallbladder as the principal cause of death. This is an incidence of 0.26 per cent, or approximately one out of every 375 cases coming to autopsy. This is the highest incidence of perforation that has been reported. Nineteen, or 43 per cent of these cases, were free perforations which without evidence of walling off had led to generalized peritonitis. Almost two-thirds of these patients were 50 years of age or more. They also found that there was a much higher proportion of male patients, 22, or 68 per cent of the patients, being men. This is of suggested importance in the consideration of the cases reported above, because all but one of these patients developing acute cholecystitis following operation unassociated with the biliary tract, were men.

Green and Coe<sup>7</sup> report perforation of the gallbladder occurring twice in the same patient. Cholecystostomy was done for the first perforation. The second perforation was followed by death. This was a free perforation of the gallbladder with an estimated 100 cc. of bile in the peritoneal cavity. The site of perforation was adjacent to an old sinus communicating with the fundus of the gallbladder. To all intents and purposes, therefore, it was a perforation at the same site, and in both instances the attacks were associated with pain radiating to the right shoulder as well as pain and tenderness in the right upper quadrant. Both were rapidly progressive.

Acute cholecystitis may be unrecognized as a complication following surgical procedures. The incidence of cholelithiasis in the population is rather large. This is especially true of those patients who are over 50 years of age. Our surgical armamentarium has resulted in an increase in the number of patients in the older age group who are daily operated upon throughout the country. The onset of pain in the abdomen localizing in the right upper quadrant, usually associated with nausea and vomiting and accompanied by some elevation of temperature and leukocytosis, would seem sufficient to make this diagnosis relatively certain. Of significance in evaluating the immediate situation is the patient's past history relative to biliary tract disease. Indeed, the patient over 50 years of age who is to undergo a major surgical procedure

for a condition unrelated to the biliary tract should have a careful evaluation of his history to determine any symptoms referable to this system. If the history is suggestive of biliary tract disease, it is well to do a cholecystogram to determine the presence or absence of cholelithiasis and the capacity of the gallbladder to fill and concentrate the dye as well as its ability to empty. Then if a patient develops the symptoms of acute cholecystitis after operation it is less likely to be overlooked if stones are known to be present.

Once the diagnosis has been established, the therapy to be accorded the patient will be determined by a number of factors. Our experience over the past 14 years at the New York Hospital justifies, it seems to us, early surgical therapy. A patient who has been operated upon and who is suffering from acute cholecystitis as a complication may not in many instances be an ideal surgical risk. It is to be expected that there will be many patients in whom cholecystectomy is contraindicated. On the other hand, there can be no contraindications to cholecystostomy done under local anesthesia. This is a minimal procedure, it is also one which may be life-saving. There are many patients, perhaps in the majority, who will recover from this attack. Many patients will refuse a second operation, and there are those for whom the surgeon will be reluctant to recommend even a cholecystostomy for one reason or another. In the relatively young patient the risk associated with non-surgical treatment is, we feel, much less than in the older age group. In those patients who are over 50 years of age the temperature, leukocyte count, and even the clinical picture frequently do not parallel the pathologic process which is taking place within the gallbladder. It is in this group in particular that we feel early surgery is imperative.

If a cholecystostomy is done it should be followed in a matter of months, with the patient as well prepared as possible, by a cholecystectomy. In this respect, the report of Green and Coe describing a patient who had an acute cholecystitis with perforation treated by cholecystostomy and who recovered and then years later experienced another episode of acute cholecystitis with perforation followed by death, is significant. One of the patients listed above (F. C. — #403668) developed an acute cholecystitis associated with a large stone impacted in the ampulla of the gallbladder eight years after cholecystostomy. These two cases are evidence in favor of cholecystectomy being done within a reasonable period after the compromise procedure of cholecystostomy.

#### CONCLUSIONS

Acute cholecystitis may occur after surgical procedures, especially in male patients who are over 50 years of age. When it does the best interests of the patient require operation. This may be cholecystectomy or cholecystostomy. The procedure is determined by the patient's condition. It will frequently be found that cholecystectomy may be inadvisable and that only a cholecystostomy can be done. This procedure may, however, be life-saving. Cholecystectomy should be done later, cholecystostomy is but a compromise procedure. It is no insurance against future episodes of acute cholecystitis or accompanying perforation that may well end fatally.

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DISCUSSION—DR HENRY F GRAHAM, Brooklyn, N Y I have had the pleasure of reading this paper in advance, so my discussion is a little prepared

Dr Glenn's theme seems to be (1) Acute cholecystitis is more apt to occur as a complication following operation for other conditions than its normal incidence as a primary disease (2) It is more apt to occur in elderly people past 50 and in males (3) He mentions, as a possible explanation of its occurrence, dehydration and medication which decreases secretion and causes concentration of thickened bile in the gallbladder which cannot easily be expelled upon food stimulation This is an interesting hypothesis but might be open to question in view of the types of cases where operation has been followed by acute cholecystitis I am convinced, however, that in many patients large doses of sedatives do have a deleterious effect (4) The diminished resistance of the gallbladder to pressure and infection following previous disease may favor perforation It would be easy for each of us to prove this by a review of his own records, and it would not be without chagrin if we look up those cases we have forgotten

I checked up on three cases One was a woman aged 56 who had an operation for appendiceal abscess Sixteen days later she complained of pain around the waist line and had induration of the epigastrium and right upper quadrant The appendiceal wound showed thick yellow pus A high temperature was thought to be due to sulfonamides The attack subsided after 12 days Two weeks later she had another attack with pain in the upper quadrant, tenderness and vomiting Empyema of the gallbladder was found at operation Another case was a man aged 45 who had suffered from epigastric pain for six months with a loss of 40 pounds in weight On his third day in the hospital, while being studied preparatory to operation for duodenal ulcer, he had a sudden attack of pain in the lower abdomen following an enema The leukocyte count was 14,000 X-rays were taken to visualize free air under the diaphragm and, finally, after 24 hours delay, because of the confused picture a cholecystostomy was performed for a perforated gallbladder

A physician, 72 years old, was under treatment for coronary thrombosis and acute diffuse nephritis After six weeks in the hospital he had pain in the gallbladder region He was observed for three weeks because of his poor condition Operation then disclosed an empyema of the gallbladder with a sealed-off perforation covered by omentum

This paper should stimulate an increased awareness of acute cholecystitis complicating other diseases and especially following operation for other conditions

# A CONSIDERATION OF PATHOLOGICAL FACTORS INFLUENCING FIVE YEAR SURVIVAL IN RADICAL RESECTION OF THE LARGE BOWEL AND RECTUM FOR CARCINOMA\*†

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THIS IS A STUDY of 200 patients operated upon more than five years ago for carcinoma of the large bowel where there was a reasonable chance of cure All of the surgical specimens were cleared and the lymph nodes were dissected under transillumination and the microscopically involved nodes were charted by a method reported to this society in 1938<sup>1</sup> The specimens used in this analysis were not always consecutive due to the work involved in the study of each one but were otherwise unselected except that the specimens from all fatalities were included This results in somewhat higher mortality figures and lower five-year survival rates

These 200 patients represent an operability rate of approximately 75 per cent Palliative resections for removal of tumor where known metastases could not be removed are not included in this group

TABLE I

200 CASES OF CARCINOMA OF THE COLON

	Per Cent
125 had lymph node metastases	62 5
114 alive 5 to 10 years	57 0
19 postoperative (hospital) deaths	9 5
8 died 1 to 5 years—not carcinoma	4 0
7 incomplete follow-ups	3 5

There is need for accurate anatomic location of tumors when discussing treatment of carcinoma of the rectum The term "rectosigmoid junction" means different things to different surgeons It can be located fairly accurately on proctoscopic examination However, it is impossible to identify on a surgical specimen Roentgenologists often consider it a region two or three inches in length This study has demonstrated the very different prognosis, recurrence, and mortality rate in different regions of the colon It seems to us that a new set of landmarks should be used We have designated those carcinomas which are partially or completely below the peritoneal reflection as "extraperitoneal carcinoma of the rectum" There were 112 of these Those lesions which are entirely covered by peritoneum, anteriorly, and which are below the promontory of the sacrum should be designated as "intraperitoneal carcinoma of the rectum" There were 41 of these Fourteen were in the redundant loop of sigmoid above the promontory of the sacrum (These last two—total of 55—will be grouped as one in this discussion as all findings

\* Read before the American Surgical Association, March 25, 1947, Hot Springs, Va

† Funds for this investigation were obtained from the Otho S A Sprague Memorial Institute Fund of the Presbyterian Hospital

were identical ) Fifteen were in the right colon, which included the cecum, ascending colon, hepatic flexure and the first three inches of the transverse colon Eighteen were in the left colon, which included all of the remainder of the colon to the redundant loop of the sigmoid

One hundred and twelve tumors were partially or completely below the peritoneal reflection There were 12 postoperative deaths and four had no follow-up Only 26 of the 69 with node metastases were alive after five years (37.5 per cent), whereas 32 of the 43 without node metastases were alive five years (74.4 per cent)

TABLE II  
112 EXTRAPERITONEAL RECTAL CARCINOMAS

	Per Cent
58 alive 5 to 10 years	51.8
12 postoperative deaths	10.7
69 had lymph node metastases	61.9
26/69 with node metastases alive 5 years	37.5
32/43 without node metastases alive 5 years	74.4

Of the 69 with node metastases, 30 or 43.5 per cent developed recurrent carcinoma in less than five years while only five or 11.6 per cent of the 43 without involved nodes developed recurrent carcinoma

TABLE III  
112 EXTRAPERITONEAL RECTAL CARCINOMAS

Recurrence	69 With Node Metastases		43 Without Node Metastases	
Local	16	23.2%	2	4.6%
Liver	11	15.9%	2	4.6%
Lung bone general	3	4.3%	1	2.3%
	30	43.5%	5	11.6%

The incidence of local and liver recurrences in these low lying tumors is striking

Fifty-five tumors were entirely above the peritoneal reflection Fourteen were in the sigmoid and 41 were below the promontory of the sacrum All findings were identical and these were grouped to save space The favorable prognosis in this group and especially in those without lymph node metastases (90 per cent), is striking

Twenty-seven of the 55 patients had obstruction resections performed In many, the extraperitonealization of the resected area was done as described by David<sup>3</sup> In the more unfavorable cases, abdominoperineal resections were performed This probably accounts for the fact that the results with obstruction resections were about the same as with the abdominoperineal resections 18.1 per cent of the 55 died of recurrence within five years, the recurrence rates being similar in the two types of operations The low incidence of

## LARGE BOWEL CARCINOMA

recurrence here contrasts sharply with the 43.5 per cent seen in tumors which are extraperitoneal

TABLE IV  
55 INTRAPERITONEAL RECTAL AND SIGMOID CARCINOMAS

	Per Cent
36 alive 5 years	65.4
4 postoperative deaths	7.2
3 deaths not due to carcinoma	5.5
2 had no follow-ups	3.6
35 had node metastases	63.3
18 with node metastases alive 5 years	51.4
20 had no node metastases	
18 without node metastases alive 5 years	90.0
1 no follow-up	
1 postoperative death	
27 obstruction resections	
18 alive 5 years	66.6
16 had node metastases	
9 with node metastases alive 5 years	56.2
2 postoperative deaths	
1 short follow-up	
11 without node metastases	
9 without node metastases alive 5 years	81.9
1 postoperative death	
1 no follow-up	

TABLE V  
RECURRENCES IN 55 INTRAPERITONEAL TUMORS

	No. Patients	Per Cent
Local	2	3.6
Liver	6	10.9
Lung or general	2	3.6
Total	10	18.1

Resections of the 33 patients with carcinoma proximal to the sigmoid colon were done by several different surgeons. Twenty-one had lymph node metastases (63.6 per cent). Twenty were alive five or more years (60.6 per cent). There were three with carcinoma of the cecum and with metastases to nodes who died after operation (9.1 per cent). One was lost to follow-up.

Fifteen were in the right colon, all had ileotransverse colon anastomoses at the time of resection. Thirteen or 86.6 per cent of these had metastases to nodes and, in spite of three postoperative deaths and one lost to follow-up, nine were known to be alive after five years (61.5 per cent). These operations were performed before the era of chemotherapy, therefore, the operative mortality in this group would be lower at this time.

TABLE VI  
15 TUMORS OF RIGHT COLON  
ALL WITH ILEOTRANSVERSE COLON ANASTOMOSES

	Per Cent
9 alive 5 years	60.0
13 had involved nodes	86.6
7 with involved nodes alive 5 years	53.8
3 postoperative deaths	
1 had no follow-up	



Eighteen tumors were in the transverse or descending colon or at the splenic flexure. Only eight had node metastases (44.4 per cent). This is the lowest incidence of involved nodes seen. Five of these eight died of recurrence within five years. Only three of the eight lived five years (37.5 per cent) in contrast to 80 per cent of those without involved nodes. All of these had obstruction resections. There were no postoperative deaths and one was lost to follow-up. This suggests that resection in this area has been too conservative.

TABLE VII  
18 TUMORS OF LEFT COLON  
ALL OBSTRUCTION RESECTIONS

	Pcr Cent
11 alive 5 years	61.1
8 had involved nodes	44.4
3 with involved nodes alive 5 years	37.5
No postoperative deaths	
8/10 without nodes alive 5 years	80.0

The surgeon gave a guarded prognosis at the time of resection because of grossly enlarged lymph nodes in 55 of the 200 cases. This chart indicates the prognosis in those having palpably enlarged nodes which are proven to have metastases on microscopic section.

TABLE VIII  
55 OF 200 GIVEN GUARDED PROGNOSIS DUE TO LARGE NODES

Location of Tumor	Alive 5-10 Yr	Died 0-5 Yr	P Op Deaths	Liver	Recurrences Local	Gen	Deaths Not Ca	Total Patients
Extraperitoneal								
With nodes	5	16	3	8	6	1	2	21
Without nodes	2	1					1	3
Below promontory								
With nodes	6	10		5	1	3	1	16
Without nodes	6							6
Colon								
With nodes	4	5	2			2		9
	<hr/> 23	<hr/> 32	<hr/> 5	<hr/> 13	<hr/> 7	<hr/> 6	<hr/> 4	<hr/> 55

Small scars ("grains of sand" nodules) were palpated in the liver in 11. These were too small and indefinite to be considered metastases. Eight lived five years. One died postoperatively. One developed a local recurrence and one died of diabetes where there was no recurrence. These small lesions are usually almost of one size and the occasional operator should not be influenced adversely when they are found.

TABLE IX  
POOR PROGNOSIS DUE TO SUSPICIOUS NODULES IN LIVER—11

8 alive 5 to 10 years
3 died in less than 5 years
1 postoperative death
1 local recurrence
1 diabetes not carcinoma

LARGE BOWEL CARCINOMA

Thirty-five of the 200 patients required resection of all or part of other structures because of firm fixation of the tumor

TABLE X  
35 CARCINOMAS REQUIRING RESECTION  
OF ALL OR PART OF OTHER STRUCTURES

	No Pts	Well 5-10 Yr	P Op Deaths	Local	Recurrence Liver	Gen	No Follow-Up
Presacral fascia	8	3	2	3			
Abdominal wall	4	3			1		
Ureter and bladder	9	2	3	1	2		1
Vagina	6	3	1		1	1	
Urethra and prostate	3	1		2			
Uterus	3		1	1	1		
Bowel	2	2					
	35	14	7	7	5	1	1

Fourteen or 40 per cent of these patients were well five years This figure would be higher today as seven or 20 per cent died postoperatively and this mortality would be favorably influenced by chemotherapy Wide excision of structures adherent to the tumor is justified by these findings

Seven patients having carcinoma below the promontory of the sacrum had metastases to lymph nodes, distal to the tumor This occurs when there is lymphatic blockade This finding reemphasizes the necessity for extensive resection in those having enlarged nodes and large tumors

TABLE XI  
RETROGRADE METASTASES TO LYMPH NODES  
IN CARCINOMA BELOW SACRAL PROMONTORY

2 with involved nodes	3 5 to 5 cm below tumor
2 with involved nodes	2 5 to 3 5 cm below tumor
3 with involved nodes	1 0 to 2 5 cm below tumor

One hundred and forty had abdominoperineal resections of the rectum Four of these were two-stage resections In two, resections of other structures made a mass of tissue too large to pull through the pelvic outlet in the male and in these the rectum was cut off just above the anus and the stump closed In all of these, there was an average of 55 3 nodes per specimen sectioned and studied microscopically One specimen contained 210 nodes, and six had 112 or more nodes each Those having an obstruction resection of the sigmoid or intraperitoneal rectum averaged 41 6 nodes per specimen and one specimen contained 102 nodes Specimens from obstruction resection of the left colon averaged 40 2 nodes each and one had 69 nodes Specimens of the right colon obtained by resection and primary ileotransverse colon anastomosis averaged 54 nodes each with one having 115 Seventy-two of the 125 specimens having metastases to lymph nodes had four or less nodes involved per specimen

In low lying carcinomas of the rectum, small high lying lymph nodes not uncommonly are found to contain metastases Figure 1 shows a specimen typical of such cases and serves to reemphasize the fact that the widest possible resection of the mesentery is needed to give a chance of permanent cure

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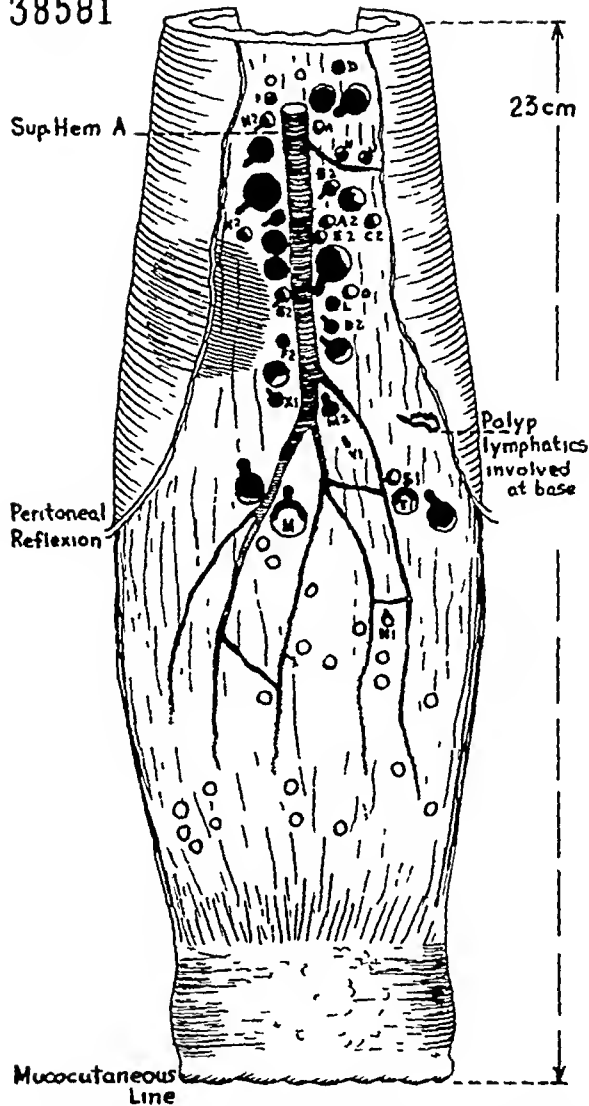


FIG 2—A 58-year-old man who had had symptoms for two months. The tumor was 5 cm above the peritoneal reflection and it involved 40 per cent of the circumference of the bowel. Abdominoperineal resection was performed. The specimen contained 60 lymph nodes and 35 of these contained carcinoma metastases on microscopic section. The nodes containing carcinoma are shown in solid black. The size of nodes and the portion of each node replaced by tumor is indicated. The tails represent lymph channels filled with carcinoma. Such channels are almost never seen except where the nodes central to the involved channels are already heavily involved with carcinoma, as in this specimen. The patient had a fatal blood transfusion reaction in another hospital two months later. Post-mortem failed to show any remaining carcinoma. Retrograde metastases occurred 5 cm below this tumor.

# LARGE BOWEL CARCINOMA

TABLE XV  
NEW TUMORS (EXCLUSIVE OF SKIN)

	Nodes at Operation	Fol. ps.	Location of New Tumor	Died	Well
1 Extraperitoneal		0	Transverse colon 7 yr		9 yr
2 Transverse colon		0	Rectum 3 yr		
			Descending colon 4 yr	5½ yr	
3 Intraperitoneal	0	0	Splenic flexure 5½ yr		5 yr
4 Intraperitoneal	0		Descending colon 4½ yr	4 yr	
				10 mo	
5 Left colon			Cecum 7 yr	8 yr	5 yr
6 Left colon			Breast 4 yr	4½ yr	
7 Intraperitoneal		0	Common duct 2 yr	3 yr	

The patient with a previous resection, either with or without a colostomy, must be watched carefully or these new tumors may cause almost complete obstruction before they are discovered

If we exclude those patients who have died of other causes without any sign of recurrent carcinoma and those who had no follow-up and those who died postoperatively, the prognosis would be

TABLE XVI  
166 CASES OF CARCINOMA OF THE COLON

	% Alive 5 Years
114 alive 5 years	68.7
58/89 extraperitoneal rectal	65.2
36/48 intraperitoneal rectal	75.0
9/11 right colon	82.8
11/18 left colon	61.1
54/100 with involved nodes	54.0
60/66 without involved nodes	90.9
26/53 extraperitoneal with involved nodes	49.1
32/36 extraperitoneal without involved nodes	88.8
18/30 intraperitoneal with involved nodes	60.0
18/18 intraperitoneal without involved nodes	100.0
7/9 right colon with involved nodes	77.7
2/2 right colon without involved nodes	100.0
3/8 left colon with involved nodes	37.5
8/10 left colon without involved nodes	80.0

The most striking finding here is in those tumors of the transverse colon, splenic flexure, and descending colon where there were involved nodes. All of these had obstruction resections and only three of the eight (37.5 per cent) were alive five years. The widest possible resection is indicated here rather than the usual V-shaped wedge of mesentery resected. The favorable prognosis (77.7 per cent) seen in right colon lesions having involved nodes is undoubtedly due to the wide resection of mesentery (54 nodes per specimen) performed when doing an ileotransverse colon resection and anastomosis.

## CONCLUSIONS

In this study of 200 patients having resection for carcinoma of the colon, there was a 96.5 per cent five-year follow-up. One hundred and fourteen were known to be alive five to ten years (57 per cent). In the study of the surgically removed specimens, microscopic sections were made of over 10,000 different

lymph nodes, carefully plotted as to location in relation to tumor and surgical landmarks. A number of facts stand out.

The lymphatic spread of carcinoma of the colon is primarily embolic. The nodes where the emboli lodge prevent further spread until the node is completely overwhelmed by carcinoma. Further embolic spread is through the

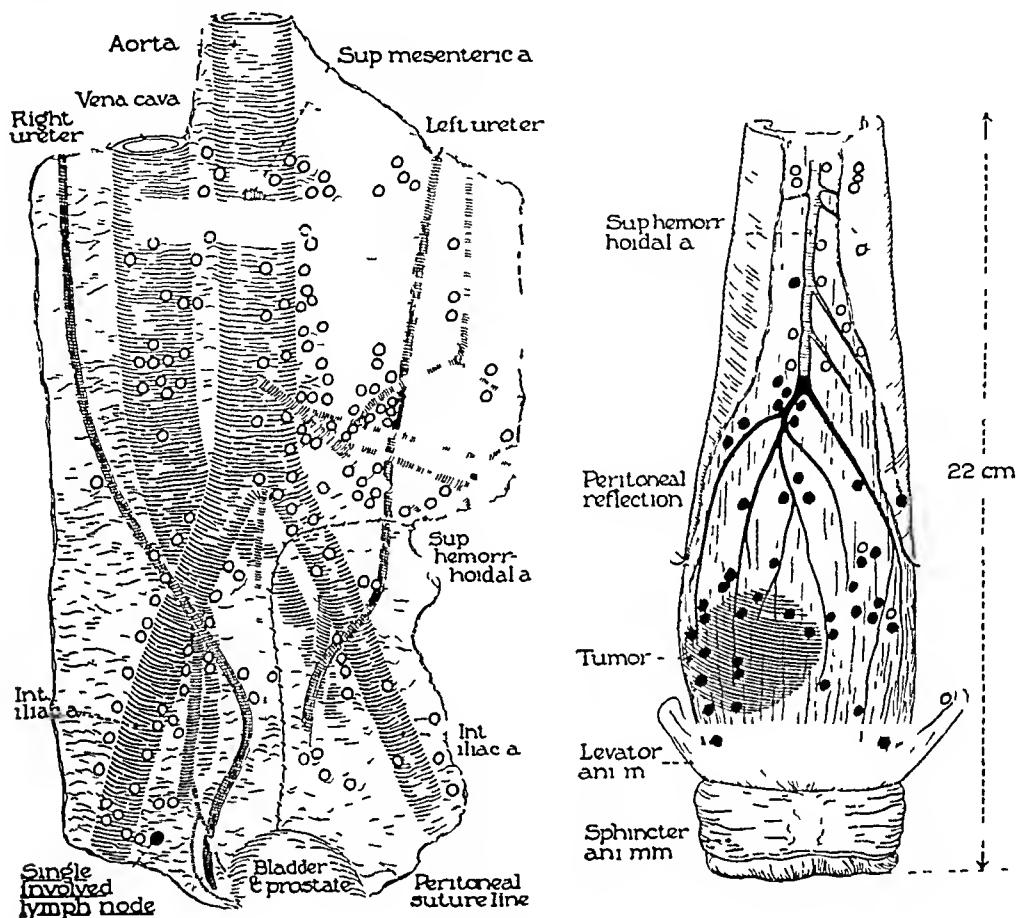


FIG 3—A 63-year-old man who had had symptoms for more than a year. This carcinoma was biopsied 12 months before, but he had refused operation. The tumor was ulcerating and it had penetrated all coats of the bowel. Nodes were palpable in the hollow of the sacrum. Sixty-two nodes were found in the surgical specimen, 43 of them showed metastases. He died of a pulmonary embolus on the 8th postoperative day. One hundred sixty retroperitoneal nodes were examined microscopically. In spite of the extensive lymph node involvement, there were no metastases above the point of resection. The one node involved was about 1 cm lateral to the widest point of resection along the levator ani muscle.

collateral channels, each new node involved tending to make a longer and more difficult channel for a new embolus to travel. Spread from one node to another does not seem to be common. Thus, the finding of a group of involved nodes within the field removable by surgery does not mean that a case is hopeless. However, it does indicate the need for the widest possible resection of lymph nodes draining the area of the carcinoma.

1. In each of the regions of the bowel studied, patients in whom no lymph node metastases could be found in the surgical specimens had a five- to ten-

year survival rate of 78.5 per cent. If those who were lost to follow-up and those who died postoperatively and of other causes after leaving the hospital were taken into account, this figure would be even more impressive (90.9 per cent)

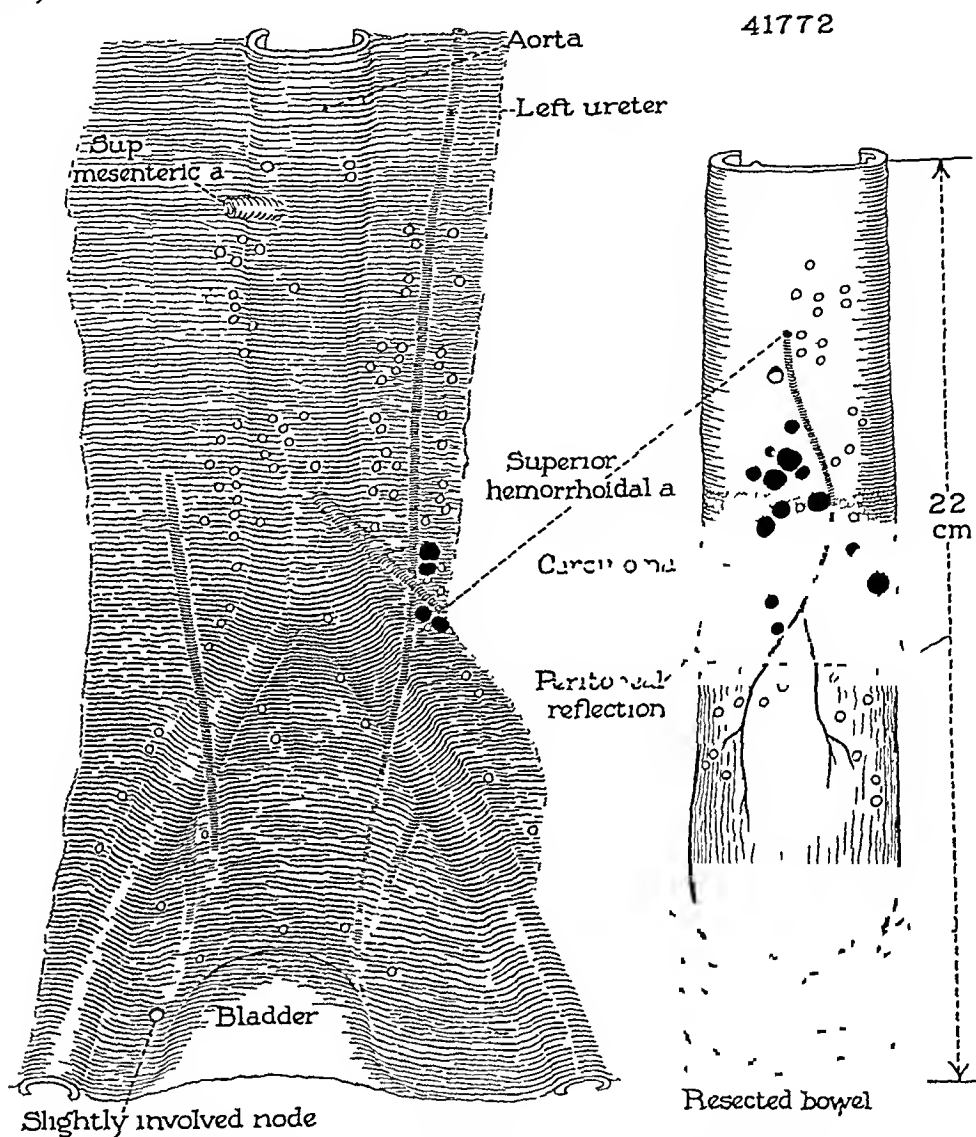


FIG 4—Seventy-two-year-old man who had had symptoms for four months. The surgical specimen contained 46 lymph nodes. Fourteen of these contained metastases. He died of pneumonia. The autopsy specimen contained 114 lymph nodes. Four nodes above and one node just lateral to the field of resection contained metastases. This is an example of metastasis laterally along the levator ani muscle as well as upward along the superior hemorrhoidal artery. In spite of a very large tumor, the lymphatic metastases were localized to an area which could have been resected.

2. Of the 125 having lymph node metastases, 56 lived five years (44.8 per cent). However, this varied depending on the location of the carcinoma. Those with carcinoma of the middle and left colon and of the extraperitoneal part of the rectum had a 37.5 per cent survival. Those of the right colon had a 61.5 per cent survival and those of the sigmoid and intraperitoneal part of the rectum had a 51.4 per cent survival rate. Several factors contribute to this difference. In the extraperitoneal part of the rectum, 23.2 per cent

developed local recurrence and 15.9 per cent developed liver recurrences. In the remainder of the bowel, local recurrences were not as easy to demonstrate since they do not cause symptoms early but they are obviously less frequent. If this incidence of local recurrence were disregarded, the prognosis in the extraperitoneal part of the rectum would be as good as in any other part of the colon.

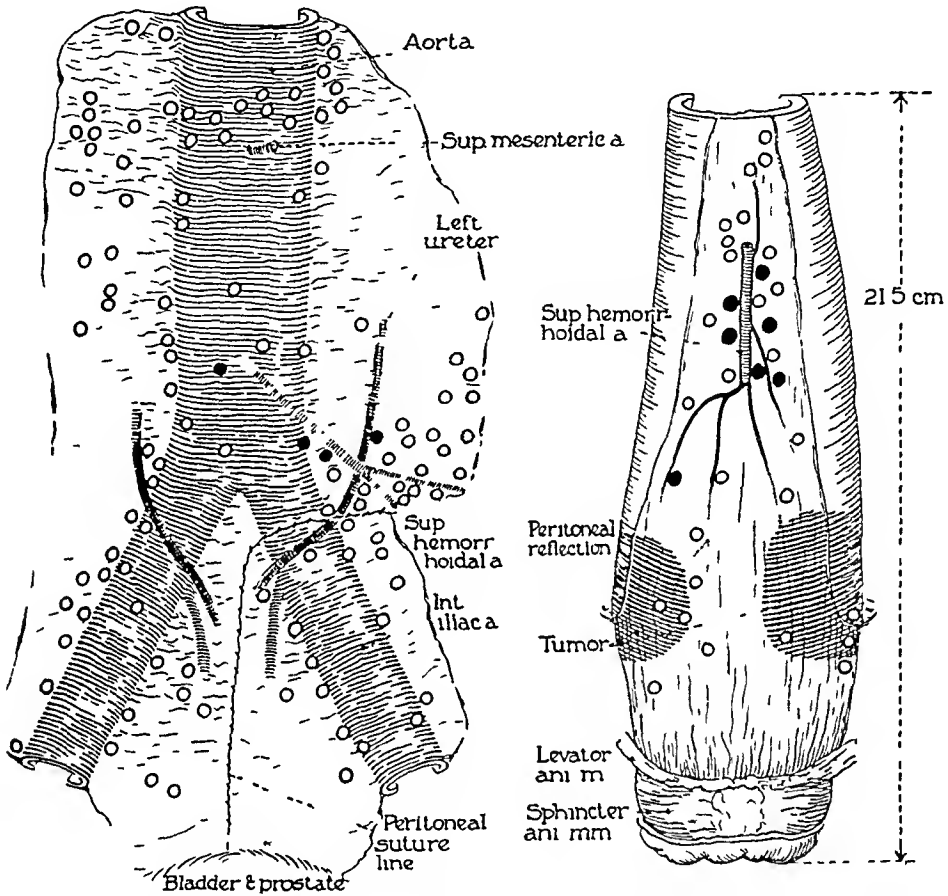


FIG 5—A 72-year-old man. He had had symptoms for six months. The surgical specimen contained 35 nodes and seven of these contained metastases. He died of bronchopneumonia. One hundred eleven nodes were studied in the postmortem preparation, four contained carcinoma. The highest metastasis was in a node found at the junction of the inferior mesenteric artery and aorta.

3. The 37.5 per cent survival rate of those having carcinoma of the left side of the colon when node metastases are present indicates the need for wider resection of mesentery in this area.

4. Resection of fixed tumors and the structures to which they are adherent give a better prognosis than might be expected, a 40 per cent five-year survival. Twenty per cent died postoperatively. This figure will be much improved when chemotherapy is used.

5. Retrograde metastases to nodes one to five centimeters below the tumor occurred in seven of the 153 tumors below the promontory of the sacrum (4.6 per cent).

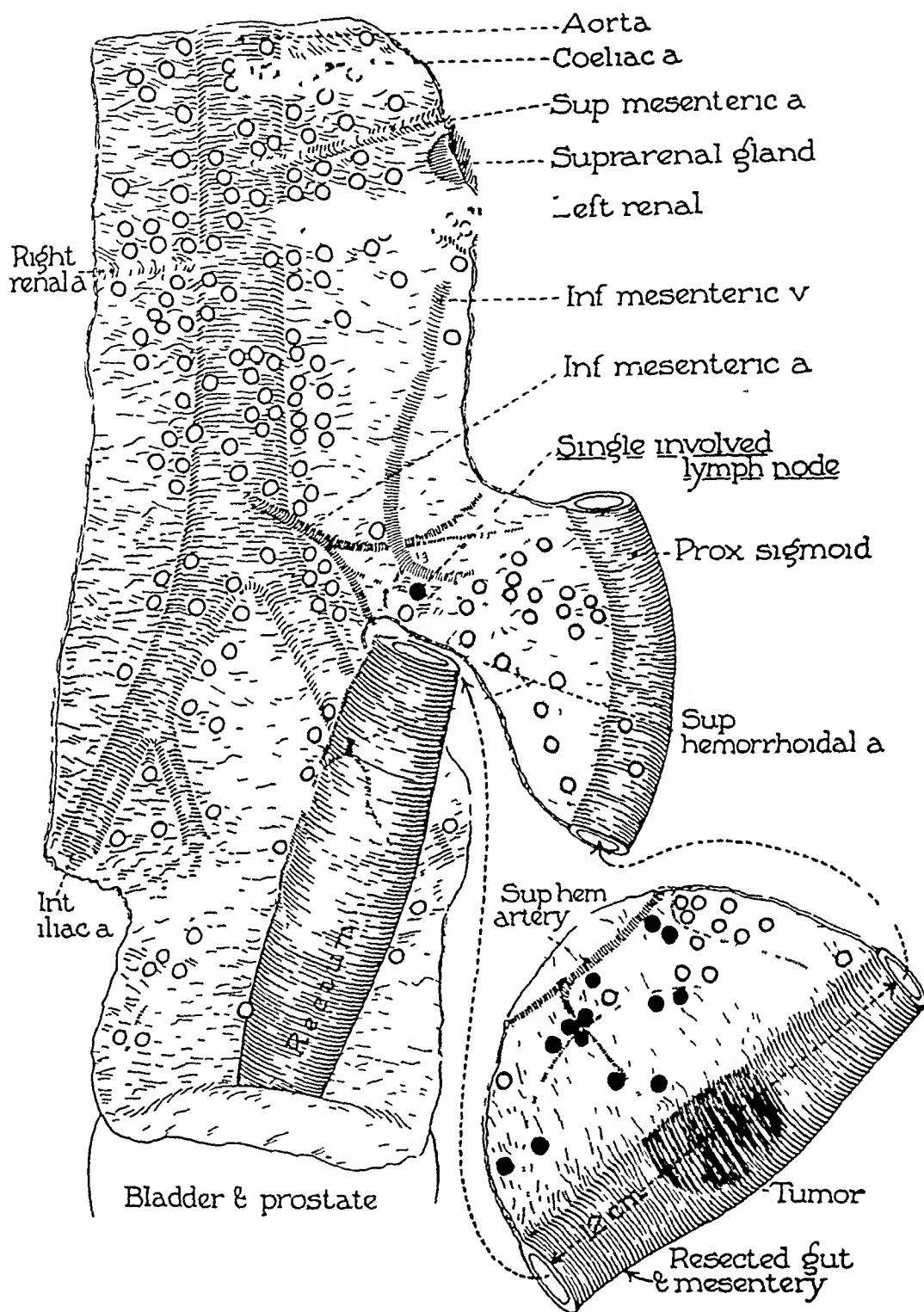


FIG 6—A 66-year-old fat man. He had had a known coronary thrombosis ten months before. The lesion was one inch above the peritoneal reflection. It was the size of a fist and there was a mass of nodes extending to the promontory of the sacrum. A David type of obstruction resection was performed. He died 14 days after surgery of myocardial failure. One hundred sixty-eight nodes were found in the postmortem preparation. The one involved node was less than 1 cm beyond the line of resection.



6 The liver was the site of recurrences in 10 per cent to 15.9 per cent of the tumors. These were probably due to blood borne metastases and bear out the figure of 15 per cent blood vessel involvement reported by Coller.

7 When small "grain of sand" nodules of a uniform size are found in the liver, the operator should not give too pessimistic a prognosis as most of these are scars.

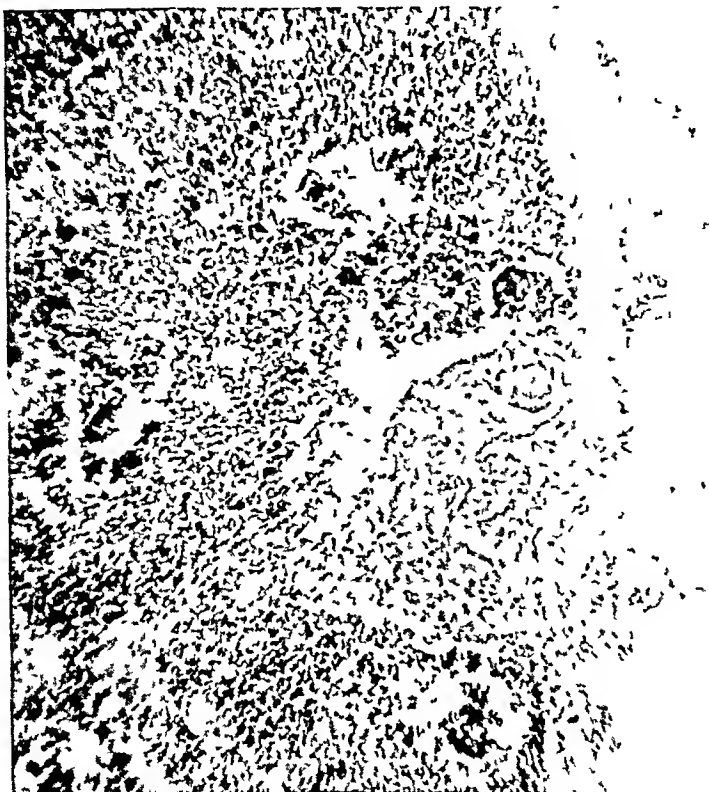


FIG 7—Photomicrograph of the entire amount of carcinoma metastasis found in the one node which was not removed in the surgical specimen.

8 Two of three patients who developed carcinoma of the rectum while pregnant lived over five years. This suggests that the gloomy prognosis given pregnant women with neoplasms may not be justified in carcinoma of the rectum.

9 Postmortem examination of those dying in the hospital after resection for carcinoma of the rectum showed that the ordinary postmortem examination will usually fail to demonstrate small metastases in the remaining retroperitoneal lymph nodes. Four of 11 who had postmortems were found to have metastases to nodes in the retroperitoneal tissues. In three of these, complete removal of all node metastases would have been obtained if the field of resection had been 1.5 cm wider.

10 It is interesting to speculate on the fate of the cancer cells left in these nodes (nine) had the patient lived. In some, inflammation might have resulted

either in death of the cells or fixation in heavy fibrous tissue. It is not unlikely that such metastases in lymph nodes missed at operation finally grow. They might grow to great size without giving symptoms. We have sections of the blood vessels supplying lymph nodes being invaded by cancer. Possibly emboli from such a source might be responsible for the sudden appearance of multiple metastases many years after resection of the primary growth.

11 New carcinomas developed in seven patients who had had resections. This does not include carcinoma of the skin. In some, the diagnosis was not made for several months after symptoms appeared. Patients who have had one cancer of the colon should be reexamined carefully whenever any symptoms suggesting carcinoma appear.

12 In evaluating the type of procedure used in treating carcinoma, the survival rate is important. Of those who died of recurrence in less than five years, two-thirds occurred within three years and one-third between three and five years. Six of those listed as five-year cures developed recurrences and were dead or dying in less than seven years. In view of the appreciable percentage who develop recurrence in the fourth and fifth year after operation, it seems foolish to consider anything less than a five-year survival as a cure. Such short term survivals should not be included in discussions since they lead the general practitioner to false conclusions.

Finally, this study indicates the need for the widest possible resection in carcinoma of the colon. Lesions which are partially or completely below the peritoneal reflection have a high incidence of local and liver recurrence and pull through or sleeve resections are not much better than a local resection. The Miles operation seems to give the best chance of cure here.

As far as lesions within the peritoneal cavity are concerned, we have performed obstruction resections on several that could be palpated when doing a rectal examination. This is justified if *not only the bowel wall* but the *blood vessels and lymph bearing tissue* are resected at least one and a half to two inches below the lesion as well as to a point just distal to the first sigmoid artery, this is a point about one and a half to two inches above the promontory of the sacrum. If this is not done, involved nodes will be missed. The David extraperitoneal procedure will allow for such a resection in many. If, after such an extensive resection of mesentery there is still an adequate blood supply to the distal loop, we will not object to end to end anastomosis. The point of the discussion about end to end anastomosis is missed, it seems to us. It should be, "Can you remove all of the cancer?" and not, "Can you sew two ends of bowel together?" Obviously, in those intraperitoneal lesions below the promontory of the sacrum which are large or have palpably enlarged nodes, the abdominoperineal resection will give a greater chance of cure.

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DISCUSSION —DR FRED W RANKIN, Lexington, Ky Dr David and Dr Gilchrist deserve great commendation for this enormously important piece of work on the lymphatic spread of rectal cancer It is an extension of earlier work done by them and, subsequently, corroborated by other workers in this country and abroad No one, so far as I know, has ever done such a meticulously painstaking pathologic examination of post-operative specimens as they have, and I think that their demonstration that the more glands one examines, the more often their extension is demonstrated, is of far-reaching significance This contribution likewise buttresses the epic work of Miles published at the turn of the century and more strongly than ever emphasizes a number of basic points dealing with the spread of cancer and directly bearing upon the type of operation indicated for eradication of rectal malignancy

1 They show conclusively that it is essential to examine a large number of glands in any operative specimen, and they have developed a method of examination which is unique and useful Their average of 55 glands per specimen is far above that of most pathologists

2 They indirectly emphasize the grade of the growth as a good yardstick whereby one measures the prognosis It has likewise been my experience that the longevity is in direct ratio to the grade of the growth and, consequently, the lower the grade, the less likely early metastasis, and the higher the grade, the more likely early metastasis

3 They clearly demonstrate that radical extirpation of rectal malignancy with a widespread removal of gland-bearing tissue gives the highest percentage of long time freedom from recurrence Even when there is no involvement about one-half of their patients have lived five years free from return This fundamental fact, which has long been applied in surgery of the breast and elsewhere, is particularly applicable in surgery for rectal cancer, since the prognosis here is so obviously superior to that of cancer elsewhere in the gastrointestinal tract

It would seem unnecessary to point out that any operation which is predicated upon any other thesis than the widespread dissection of gland-bearing areas with the growth is excessively vulnerable In operations for cancer of the rectum my own choice has been for the past fifteen years the one-stage combined abdomino-perineal resection after the technic of Miles

Increasingly better preparatory measures, a more thorough understanding of a balanced physiologic equilibrium, and more meticulous attention to technical details have widely extended the scope of this operation In a recent review of 167 cases of my own done between 1934 and 1941, and whose postoperative ages therefore run from seven to 13 years, I have found 55 per cent of them alive and free from recurrence as of this date The operative mortality in this group was 5.3 per cent and the resectability rate was 74 per cent It is interesting to note two other cases which I have seen in my service in the last year with recurrences in the posterior vaginal wall following the Miles' operation one of these cases done by me and one done by another member of this Association three and four years ago respectively This evidence that there is a downward spread of lymphatics through which cancer occasionally metastasizes is definite, I think, and although it is a small group, it has a direct bearing on the prognosis Moreover, it is generally recognized that lateral spread into the ischiorectal fossa occurs in a really larger group of cases, and this, I think, necessitates a widespread removal of the levator muscles Most important, however, the greatest spread of rectal cancer is upward into the mesentery of the sigmoid and these tissues may be removed radically only by some operation which includes a colostomy

The recent rediscovery of the pull-through operation and the great emphasis placed by some surgeons on technical procedures which decry the sacrifice of the sphincter mechanism of the rectum make it important, I think, that experienced surgeons point out again and again the limitations of such types of operations in the vast majority of cases Technically the operation is not difficult, but that actually is hardly the important consideration Actually, one must ask of any operation for cancer how many patients are alive following it at any given time? That is the true test of a surgical procedure For my

own part, I agree with David and Gilchrist that the sphincter-saving operations are little more than local excisions for all cancers situated below the peritoneum

I had thought that the question of colostomy had been settled definitely 20 years ago, but apparently a new generation insists on a re-exploration of an already discredited field. It seems to me of utmost importance that the limits of operation be extended as widely as possible and that local attachment and metastasis do not always preclude resection, for only by radical and courageous surgery will the horizon of curability in cancer of the rectum be extended

DR THOMAS E. JONIS, Cleveland, Ohio I merely want to call attention to one figure in Dr Gilchrist's statistics, namely, that 22 per cent of these cases with lesions in the ampulla had local recurrence. Miles went to this operation primarily for that reason, because of the tremendous number of local recurrences in the perineum which followed previous lesser procedures. This figure of 22 per cent would seem a little high but it proves further that radicalism is necessary and that revival of the pull-through operations and low anastomosis will be short-lived

DR RICHARD B. CATTELL, Boston, Mass This report of Drs David and Gilchrist, together with their previous studies, has added a great deal to our knowledge of lymphatic spread of carcinoma of the colon and rectum. Their method of clearing their operative specimens for demonstration of all nodes is the most accurate method of determining the extent of lymph node involvement. It should be pointed out that this information in the individual case is not available at the time the surgeon makes the decision regarding the extent of the resection. This must be based on the operative findings

In a review of 114 patients with carcinoma of the rectum operated upon at the Lahey Clinic in 1945, we found a preponderance of cases with extensive involvement. Only 39 had the lesion confined to its primary site. Regional nodes were involved in 24. Local extension occurred in 11, while 14 had direct invasion of other organs, not including 26 who had liver metastases. We were unable to determine by operative exploration the extent of the spread. Because of this experience we believe that abdomino-perineal resection is necessary to offer the greatest chance for cure

In a previous study of five-year results, we found that 80 per cent were free of recurrence when there was no spread, while if lymph node involvement was found, this figure dropped to 30 per cent. If blood vessel invasion could be demonstrated, the five-year survival rate was 15 per cent

Dr Colcock, of our surgical staff, has recently completed a ten-year follow-up study of patients having resection for carcinoma of the rectum. When lymph nodes were not involved, 60 per cent survived five years and 51.8 per cent survived ten years, yet when lymph nodes were involved, 30.2 per cent survived five years and 23.2 per cent survived ten years

We are confronted with the fact that the majority of patients who have cancer of the rectum have extension of their disease beyond the primary site. We must not lose sight of this fact in planning our operative procedure. The best results should follow the most radical procedure, that of abdomino-perineal resection

DR OWEN H. WANGENSTEIN, Minneapolis, Minn Inasmuch as President Churchill has asked whether there is anyone here to speak for the more conservative operation in which continuity is re-established, I come forward only in response to that request. In doing so, I admit freely that, in low-lying rectal lesions less than 6 cm from the external anal orifice, the sphincter-saving operation should not be done. And especially in large ampullary lesions in juxtaposition to the levators, the conservative operation is out of order—a confession that I have made already elsewhere (*Surg Gyn & Obst* 81:1, 1945)

You can overdo anything—even a good thing such as the abdomino-perineal operation! I have no quarrel with the thesis that, from the point of view of curing cancer of the rectum, there is no operation superior to the abdomino-perineal operation. However, it is not a light matter to deprive a man of his rectal sphincter. It is perhaps an advice

more easily given than accepted. Moreover, surgeons cannot make a sphincter and one cannot be bought in any market at any price. Continence of feces without the internal sphincter of the rectum does not exist and operations which destroy or remove the internal sphincter fail to preserve continence.

The difficulty of the matter is, we are all such poor prophets. If one could only know with assurance that he is not depriving his patient of his rectal sphincter unnecessarily or, on the other hand, that sacrifice of the rectal sphincter is mandatory to cure the cancer—if these unknowns could be resolved, then a surgeon could always choose the right operation. Dr Gilchrist states that he has had a local recurrence incidence of 22 per cent in the abdomino-perineal operation for rectal cancer. And this, of course, is the experience of all surgeons in operating for cancer. There is no one operation that will cure all cancers. What our local recurrence incidence has been in the 60 to 70 patients upon whom we have performed the more conservative operation, we do not yet know. Despite the circumstance that I have a number of patients who are well without evidence of recurrence after excision of lesions lying 4 to 6 cm from the anal orifice, nevertheless I have learned the bitter lesson that it is unwise to attempt to salvage the sphincters in such low-lying lesions. If one does so, he compromises on the cure of the cancer. With reference to lesions in the rectosigmoid, however, I have the impression that as satisfactory an operation for cancer can be done for lesions here with restoration of continuity as with the more radical abdomino-perineal operation.

Surgeons should be consistent, though Emerson once said that "consistency is the hobgoblin of small minds." Those who affect to believe in the wisdom of excising greater lengths of intestinal segments as well as wider excision of lymphatic areas of spread should not be advocating the exteriorization operation for cancer of the colon. My associate, David State, has recently suggested in doing the Miles operation for cancer of the rectum in patients exhibiting lymph node involvement near the origin of the inferior mesenteric artery, that the mesentery of the entire left colon be excised, establishing the colostomy in the transverse colon. In cancers of the descending colon, more often than not, I mobilize both the splenic and the sigmoid flexures and anastomose the transverse to the pelvic colon. On a few occasions, because of the extent of lymph node involvement, I have excised the right colon as well, anastomosing the ileum end-to-end to the terminal pelvic colon. I have been led to do this in seeing patients with recurrent cancer around the left ureter and even the aorta a few years after local excision of lesions in the descending colon. Certainly, such a lesion should not be treated by the exteriorization operation.

In conclusion, I would suggest that, a tempered ambition to save the rectal sphincter as well as to cure the cancer, is a praiseworthy objective in *suitable* cases of cancer of the upper rectal ampulla and most, if not all, removable cancers of the rectosigmoid.

DR LEO ELOESSER, San Francisco, California. Just a small voice from the wilderness. I am inclined to disagree with both Dr Gilchrist and Dr Wangenstein on one point, viz, I think one has to consider not only how *long* one's patients are going to live, but *how* they are going to live. There is little doubt that an abdomino-perineal excision with permanent colostomy may assure a maximum percentage of freedom from recurrence in low-lying cancer of the rectum. However, I think that some of us might be inclined to forego this maximum and accept a 10 per cent or so of risk—a risk of living a few less years with a normally functioning anal sphincter, instead of eking out a few more years of life embarrassed by colostomy.

DR R. KENNEDY GILCHRIST, Chicago, Ill (closing). The most interesting fact in this study has been the percentage who had five-year survival even in the days before chemotherapy. As our studies progressed, we have become more and more radical in our resection of the lymphatics draining the carcinoma, and I feel certain that a study of those cases done in the last five years will show an even more favorable percentage of five-year cures.

## ADJUVANTS TO SURGICAL THERAPY IN LARGE BOWEL MALIGNANCY\*

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THE TREATMENT OF MALIGNANT LESIONS of the large bowel presents a multitude of problems about which there is no unanimity of opinion. Surgeons are not agreed on what constitutes operability, whether radical operation should be done in the presence of major metastases, the advantages of a one-stage over a two-stage operation, aseptic versus open anastomosis, or various modifications of the Mikulicz operation versus end-to-end or end-to-side anastomosis.

The well known caution of our profession has often led us to be slow in adopting concepts and procedures which may have much to commend them. Brunschwig<sup>1</sup> has recently summarized the concept of radical surgery as follows: "The advocacy of a more radical surgical attitude in regard to advanced abdominal cancer is not to be interpreted as justification for indiscriminate radical operations. In appreciably extending radical surgery, proper selection of patients is of utmost importance. By persistent and concerted efforts in these directions, surgeons will contribute in their field to the general advance in the cancer problem." With this statement we agree. With its acceptance many lesions which have previously been considered inoperable become operable.

The answer to many of the problems which confront the surgeon interested in malignancy of the colon is not to be found in statistical analysis alone, however useful this tool may be when used within its limitations. Operability will vary with the skill and boldness of the surgeon, the method of operation frequently varies with training and experience. Both may be influenced by attention focused upon the immediate mortality rather than upon the five and ten year cures, however few they may be.

We propose to present a few adjuvants to surgical therapy which we and others have found to be useful.

### ANEMIA AND HYPOPROTEINEMIA

Anemia is frequently observed in association with neoplasms of the large bowel. It is seen in the most advanced type in certain instances of large bowel polyposis and in cancer of the cecum and ascending colon. In the latter site it may be so severe as to simulate pernicious anemia.

Many of these patients are also in poor nutritional condition, a circum-

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\* Read before the American Surgical Association, March 25, 1947, Hot Springs, Va.

stance brought about by an inadequate intake of foodstuffs and at times by an exorbitant loss of protein in the stool during periods of diarrhea. Thus malnutrition and anemia are often found to exist in the same patient (Fig 1).

When hypoproteinemia and anemia are present, the circumstance is a complex one. George Whipple<sup>2</sup> has described this state as follows: "We believed that in a dog, both anemic and plasma depleted, we could influence the protein flow toward hemoglobin by one food factor or toward plasma protein by another food. To our surprise we observed that such dogs

### =====Anemia and Hypoproteinemia=====

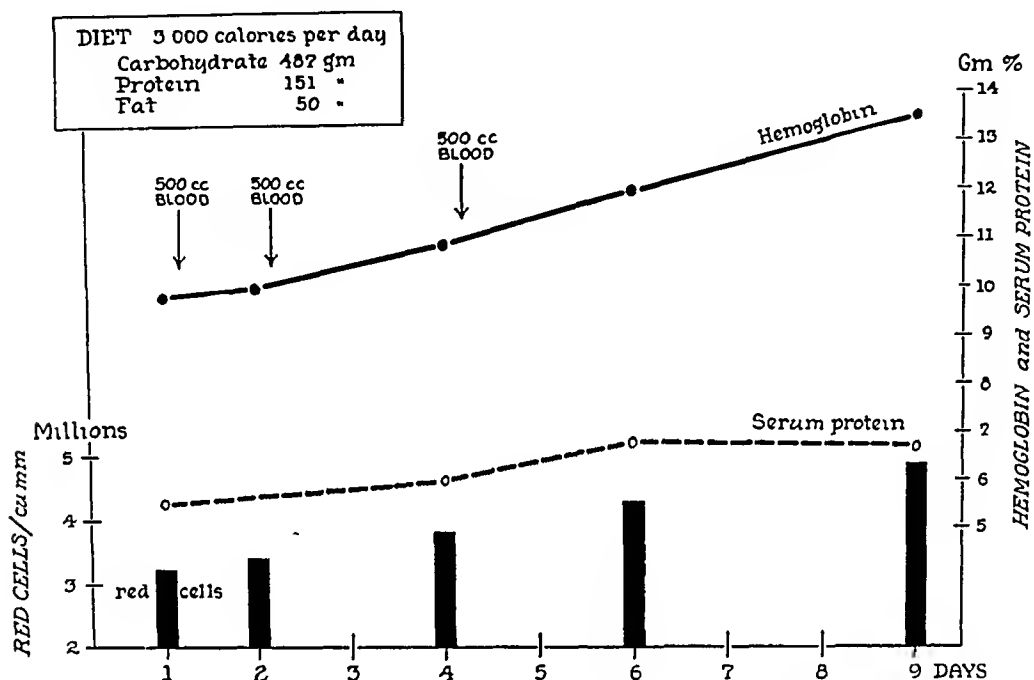


FIG 1—Coexisting anemia and hypoproteinemia corrected by transfusions and diet

(hemoglobin and plasma protein deficient) always produce more hemoglobin than plasma protein no matter what diet protein is used. Hemoglobin in its production may draw on the plasma protein but hemoglobin stands apart in the protein economy and does not contribute freely to the protein pool. The body guards jealously the fabrication of hemoglobin and given a real need for both plasma protein and hemoglobin the protein flow favors hemoglobin, which under these circumstances is produced in more abundance than the plasma protein."

Every possible effort should be made to correct an existing anemia in protein deficient patients in whom attempts are being made to correct the protein deficiency. Patients presenting both anemia and hypoproteinemia should be transfused vigorously prior to operation. This was repeatedly demonstrated in patients during World War II. Dependence for the correction of the nutritional defect could not be placed on diet, minerals or small

transfusions, for even under these circumstances the protein and minerals ingested went first to provide the components necessary for the synthesis of hemoglobin and not to replace the depleted stores of body and plasma protein

We<sup>4</sup> have shown, as have others, that the hypoproteinemic dog is more susceptible to hemorrhagic shock than is the normally nourished dog, and no one would question the increased susceptibility of the undernourished patient to traumatic or hemorrhagic shock (Fig 2) The anemic patient is likewise

**The Loss of Blood Necessary to Reduce the  
Blood Pressure below 60 mm Mercury  
for Thirty Minutes**

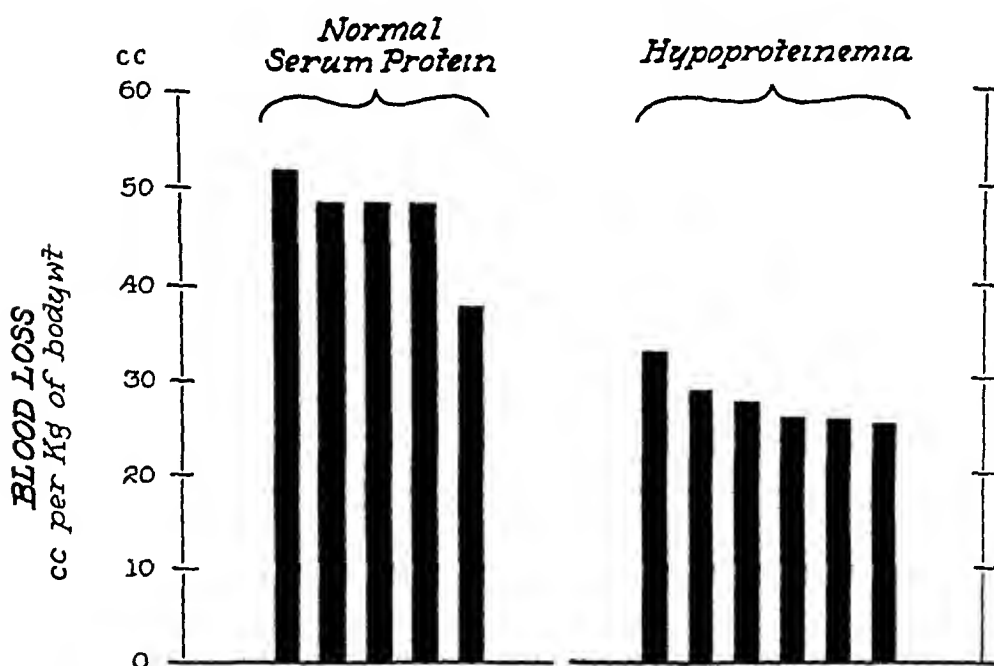


FIG 2—The loss of blood necessary to reduce the blood pressure below 60 mm of mercury for 30 minutes in hypoproteinemic dogs and dogs with normal serum protein levels

more susceptible to shock from trauma or blood loss Furthermore, the nutritionally deficient patient is more susceptible to faulty wound healing, wound infection and exaggerated edema following trauma at sites of anastomosis In protein deficient patients improved protein nutrition has been shown by Cannon<sup>4</sup> to increase antibody formation and the production of phagocytes, thus strengthening two biologic factors which assist in the control of invasive infection Cannon and his associates<sup>5</sup> have called attention to the fact that in severe malnutrition the cellular tissues which supply phagocytes in large numbers undergo atrophy

#### VITAMINS

Thiamin niacin and riboflavin are concerned with the intermediate metabolism of carbohydrate<sup>6, 7, 8</sup> and riboflavin is also concerned with the utilization of amino acids<sup>9</sup>



The more or less general adoption of oral chemotherapy prior to bowel resection has been most helpful, but is attended by some risks unless the collateral effects of such therapy are more generally understood

The drugs of the sulfonamide class, when given orally, demand an increase in the intake of certain vitamins. Sulfasuxidine is now widely used in the preparation of patients for resection of the colon, but it must always be remembered that within four to six days after such therapy is begun the thiamin



FIG 3—Miller-Abbott tube passed through the small intestine prior to resection of the colon

output in the feces will reach a zero level unless the thiamin intake in the diet is greatly augmented<sup>9</sup>

The physiologic requirements of certain vitamins are met in large part by the absorption of vitamins synthesized in the bowel as the result of bacterial metabolism<sup>10</sup>. The chemotherapeutic agent, be it a sulfonamide or an antibiotic, reduces to a variable degree the bacterial growth, but the effectiveness in such action is attended with a reduction in the intestinal vitamin synthesis. Oral sulfonamide therapy may result in a definite reduction in the synthesis of vitamin K in the intestine with a resulting hypoprothrombinemia<sup>11, 12</sup> and

## LARGE BOWEL MALIGNANCY

hemorrhage at the suture line. Oral streptomycin therapy would similarly effect the bacterial synthesis of vitamin K.

### LONG TUBE DECOMPRESSION

In 1940 William Osler Abbott and one of us<sup>13</sup> reported our early experience on the use of the Miller-Abbott tube as a means of facilitating a one stage resection and anastomosis of the right colon (Fig 3). The method has also been favorably reported upon by Allen Whipple<sup>14</sup> and by Newton and Blodgett<sup>15</sup>. Our experience with its use in resections of the right colon was so satisfactory that two stage resections of the right colon have not been done in our clinic since 1938.

We have since extended its use to the preparation of patients with lesions in the more distal segments of the large bowel. The tube does not always go through the ileocecal valve but it frequently does, and in our hands at least has frequently obviated the necessity of a proximal colostomy, except where acute obstruction or marked chronic obstruction was present.

The tube is passed 48 hours before the contemplated operation, and its position is checked at intervals by fluoroscopic study. Feeding and chemotherapy are continued during this period. The tube remains in the bowel after operation until the patient's intestinal functions have returned to normal. Its use in our hands has contributed to a reduction in the over-all mortality.

### CHEMOTHERAPY

The use of oral sulfonamides, especially sulfasuxidine and sulfathalidine, in the pre-operative period prior to bowel resection is now more or less generally accepted. These drugs have been useful in reducing the total bacterial population, but their action on the intestinal bacteria is highly selective and in the occasional patient the usual, or even larger, doses are without any marked effect.

More recently we have used streptomycin in these patients. This antibiotic is effective, in part at least, against all of the common intestinal pathogens. When given by mouth in a dosage of 0.25 Gm. every six hours the feces are

TABLE I  
EFFECT OF STREPTOMYCIN AND SUCCINYL-SULFATHIAZOLE  
ON THE NUMBER OF B. COLI PER GRAM OF FECES

Agent	Before	After 8 Days	After 8 Days in 85% of Patients
Streptomycin	74,836,060 000	418 000	262
Succinylsulfathiazole	23,700 000,000	150,000 000	98 857

free of the *Streptococcus fecalis* in eight days, and there results a marked reduction in the coliform group and the anaerobic organisms of the Welch type (Tables I, II and III and Figures 4 and 5). We are now studying the effect of 5.0 Gm. daily to determine whether bacterial control is achieved in a shorter period of time.

In nearly every one of the earlier reported series of resections of the colon, the mortality from peritonitis was approximately 50 per cent. Chemotherapy by any method now known does not provide sterilization of the feces, but it usually does produce a marked reduction in the bacterial count of the pathogens.

In the immediate postoperative period we have administered penicillin

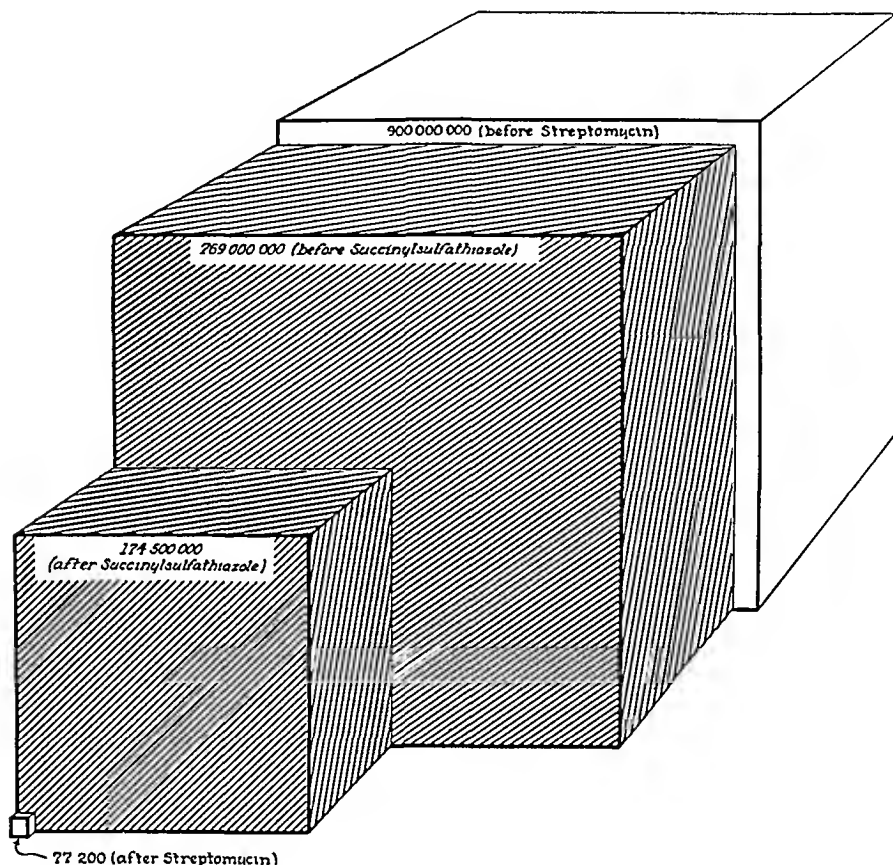


FIG 4—Relative effect of streptomycin and succinylsulfathiazole on the number of *Streptococcus fecalis* organisms per gram of feces

and streptomycin in a further effort to prevent serious peritonitis. Data soon to be reported by Zinsser and Zintel<sup>16</sup> have shown these two antibiotics to be useful in preventing spreading peritonitis following peritoneal soiling.

#### DISCUSSION

Even though a clean bowel and an empty bowel was not obtained by the adjuvants described in this paper, minor fecal contamination of the peritoneum at operation did not prove serious and peritonitis has not been the cause of a single death in the year 1946 during which time 53 colon resections were done, 40 in one stage (Table IV). Eighteen of the latter were performed by the open method. Prior to the adoption of the complete program as

# LARGE BOWEL MALIGNANCY

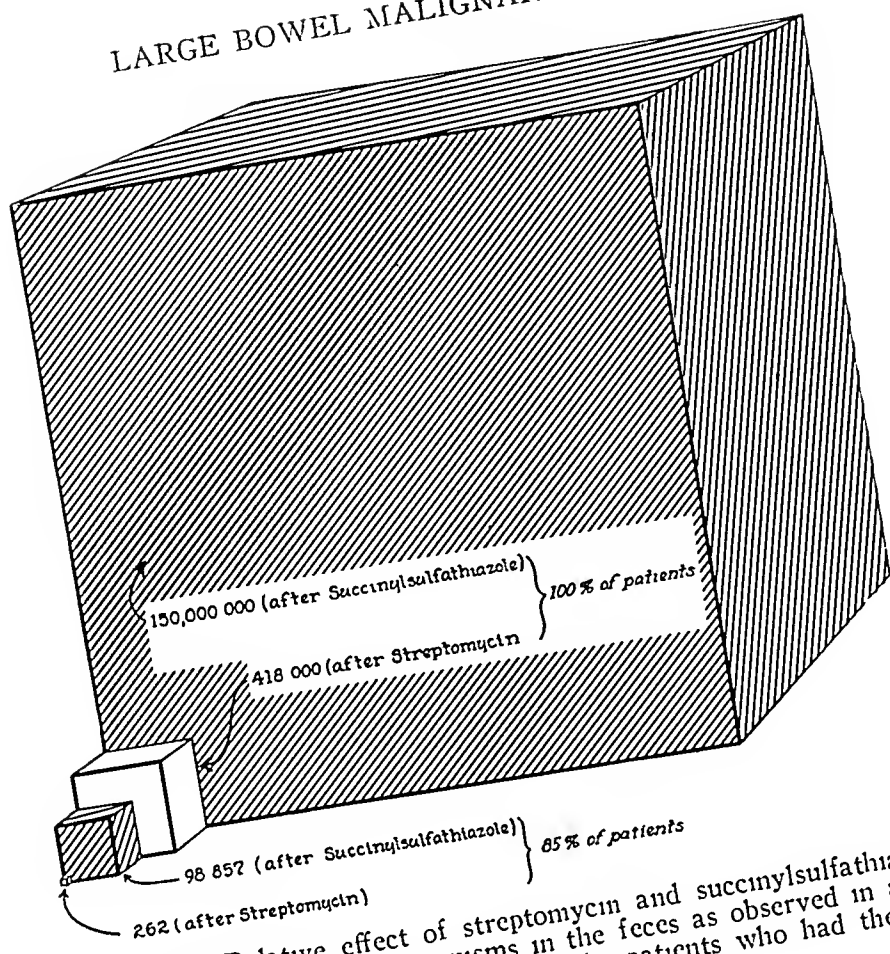


FIG 5—Relative effect of streptomycin and succinylsulfathiazole on the number of *B. coli* organisms in the feces as observed in all of the patients and in the 85 per cent of the patients who had the best results

## COLON SURGERY Operative Mortality by Years

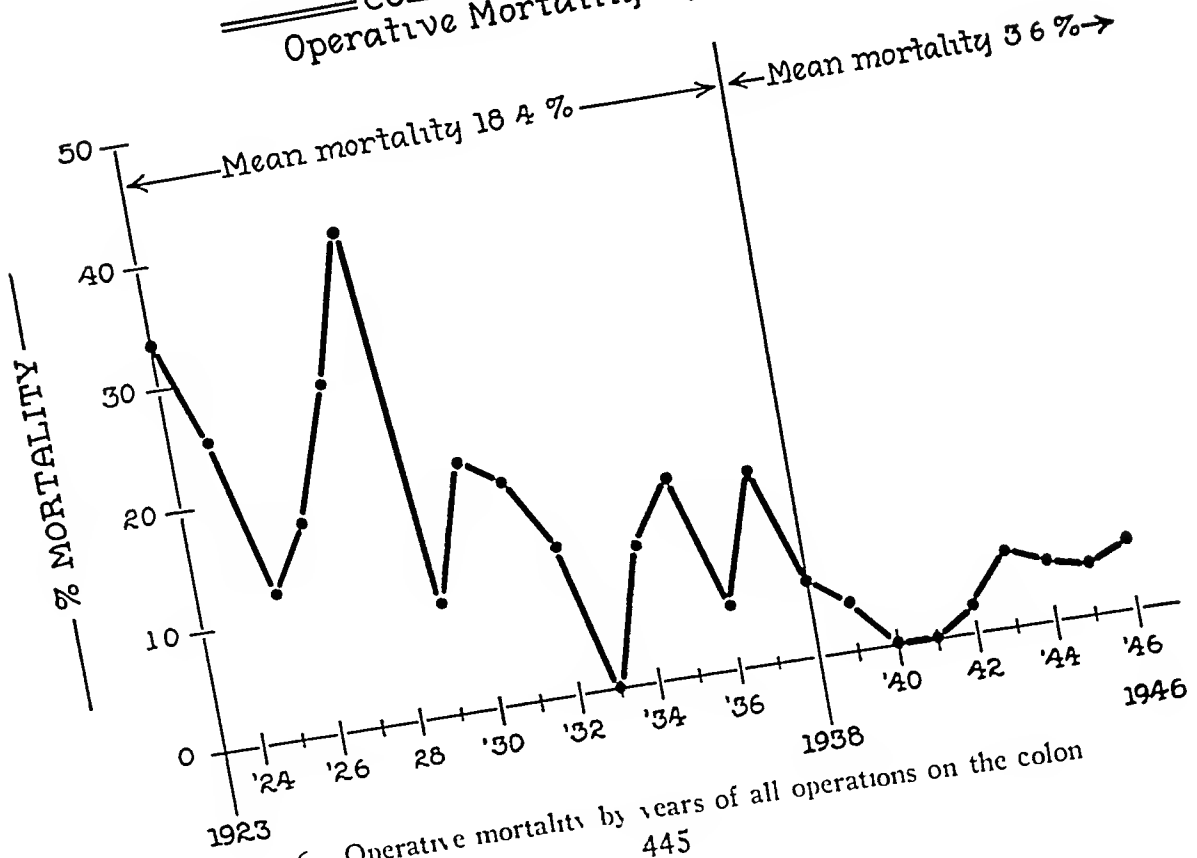


FIG 6—Operative mortality by years of all operations on the colon

described total resectability for colon cancer was 64.5 per cent. During the year 1946 total resectability was 73.6 per cent. The mean operative mortality for all operations on the colon, including perforation and obstruction, from 1923 to 1938 was 18.4 per cent, and since 1938 when we began the use of a definite portion of the program, the mean mortality has been 3.6 per cent.

TABLE II  
EFFECT OF STREPTOMYCIN AND SUCCINYL-SULFATHIAZOLE ON THE  
NUMBER OF STREPTOCOCCI FECALIS PER GRAM OF FECES

Agent	Before	After 8 Days	After 8 Days in 85% of Patients
Streptomycin	900 500 000	77 200	0
Succinylsulfathiazole	769 000 000	174 500 000	141 157 833

TABLE III  
EFFECT OF STREPTOMYCIN AND SUCCINYL-SULFATHIAZOLE ON THE  
NUMBER OF CLOSTRIDIAL ORGANISMS PER GRAM OF FECES

Agent	Before	After 8 Days	After 8 Days in 85% of Patients
Streptomycin	33 030 000	539 900	200
Succinylsulfathiazole	15 090 000	1 047 000	71 218

TABLE IV  
MALIGNANT LESIONS OF THE COLON  
JANUARY 1 1946 TO DECEMBER 31 1946

Resections of the colon	53	
One stage	40	(74.1%)
Open anastomosis	18	(33.96%)
Mortality entire group	3.8%	
One death open anastomosis		

(Table IV) In only two years prior to 1938 was the mortality ever as low as it has been in any year since 1938.

Resection with end-to-end anastomosis is supplanting Mikulicz types of resection in our clinic. One-stage procedures have entirely supplanted multi-stage operations except in the presence of perforation or obstruction.

Nothing we have mentioned replaces the gentle handling of the bowel, the greatest care in the conservation of blood supply, the prevention of major soiling and the careful approximation of the bowel edges. But when all of these have been done, a number of patients will lose their lives from peritonitis from one cause or another. The adjuvants here reported have permitted a larger number of one stage in place of multistage operations reducing the risk of secondary anesthetization, and they have led to a more rapid recovery and a shorter period of disability and hospitalization in a larger number of patients. They have led to a substantial reduction in the mortality following operations on the colon and have, we believe, played an important part in the very marked reduction in the incidence of fatal peritonitis following resection of the large bowel.

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# OBSERVATIONS ON MORTALITY FROM ACUTE APPENDICITIS AT A UNIVERSITY HOSPITAL, 1916 TO 1946\*

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THE PRESENT STUDY OF ACUTE APPENDICITIS mortality at Presbyterian Hospital, New York, is a continuation of a previous report,<sup>1</sup> and now comprises a 30-year period. The fact that 1946 marked the 60th anniversary of the first successful appendectomy performed in this country (Richard Hall<sup>20</sup> at Roosevelt Hospital, N Y, on May 8, 1886) made it seem timely to give pause and review our own results in the treatment of this surgical disease. In addition, such a study serves as a good yardstick in evaluating the work and ability of a large hospital staff. Since 1936 our records also include all cases of acute appendicitis at Babies Hospital, together with those that occasionally develop in Sloane Hospital for Women, the Squier Urological Clinic, and the Neurological Institute.

During this span of years there have been many attending staff members, interns, house surgeons, fellows, residents and assistant residents. For this reason, the results and remarks, herewith presented, are not comparable to those of individual series, or of small groups of well trained experienced, skillful surgeons.

It is proposed to present our mortality charts with appropriate comments, together with a brief discussion of the fatalities in each subgroup during the last five-year period (war years), to make a few general remarks, to offer some practical suggestions in operative therapy, and finally to submit a plan for further reduction of appendicitis mortality, at this institution.

The classification of our cases has followed the nomenclature in our previous report so as to lend continuity to the present study and therefore the descriptive pathology of each subgroup need not be repeated here. With few exceptions,\*\* the basis of our classification rests chiefly on the gross operative findings. This is quite important, because, if, for instance, a patient discloses an acute local peritonitis at operation, and subsequently dies of a generalized fibrinopurulent peritonitis, the death is placed in the former category where it will arouse greater attention and scrutiny. It is useful, too, in evaluating and interpreting end results. Classification of acute appendicitis on a time basis seems unsatisfactory because this disease does not progress at a steady even pace.

Many large clinics and hospitals follow a classification of their own choosing so that it is quite difficult to make relevant comparisons. Sometimes the use of the same descriptive term will reveal considerable differences in the

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\* Read before the American Surgical Association, March 25, 1947, Hot Springs, Va.

\*\* A few deaths are included in this series where patients were so moribund that operation was entirely out of the question.

interpretation of the pathology applied to it. Comparative figures, therefore, have not been extensively employed in this report.

The accuracy of any classification, dealing with acute appendicitis is open to criticism, and the reader may justly challenge the correctness of our findings. There are at least three factors of error. In the first place, many observers have pointed out that a classification, such as ours, is not feasible if the operation is properly executed. Secondly, there are many instances of transition from one pathologic subgroup to a succeeding one, so that a surgeon

FIG 1

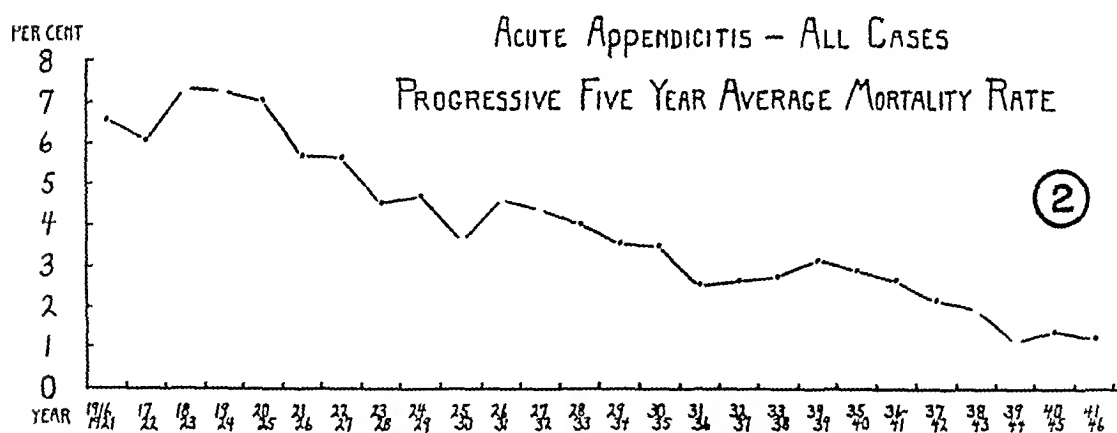
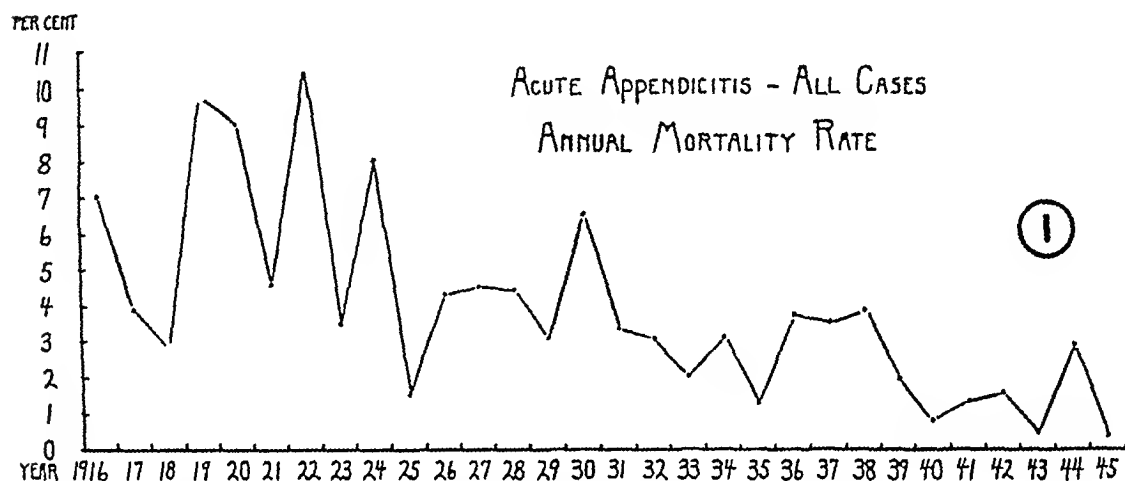


FIG 2

FIG 1—Graph showing the total annual death rate from 1916 to 1945, inclusive, in 5405 cases of acute appendicitis with its associated lesions. Total number of deaths, 193; total mortality rate, 3.55 per cent. Mortality rate for 1945 was 0.43 per cent.

FIG 2—Graph for comparison with that in Figure 1, showing the total progressive five-year average death rate from 1916 to 1945, inclusive, for all cases of acute appendicitis with its associated lesions. Mortality rate for 1941 to 1946 was 1.37 per cent.

might assign a given case to subgroup A, whilst another operator confronted with similar findings, might place it in subgroup B. Lastly, each case history is subject to interpretation and classification by the present writer, although, in doubtful instances, an effort is made to consult the operating surgeon. It is



acknowledged, therefore, that the various subgroups may be slightly inaccurate. Nevertheless, the total mortality figures (the sum of all subgroups) can be accepted as reasonably accurate.

Not only will the annual mortality curves be shown, but the corresponding progressive five-year averages in addition. The latter are considered important because they eliminate the factor of annual fluctuation, thus providing a measure of predictability and an indication of certain trends.

#### ACUTE APPENDICITIS AND ITS ASSOCIATED LESIONS ALL CASES

From 1916 to 1946 there were 5,405 cases of which 193 died. The total death rate was 3.55 per cent. The annual death rate (Fig. 1) shows considerable fluctuation but there is a definite downward trend, with 1945 showing

TABLE I

TOTAL MORTALITY RATES ALL CASES OF ACUTE APPENDICITIS AND ASSOCIATED LESIONS REPORTED IN LITERATURE

Year of Publication	Author	Place	Period Studied	No of Cases	Mortality per cent
1938	Ray <sup>41</sup>	New York Hospital N Y	1932-1937	886	2.1
1938	Turner <sup>37</sup>	London Hospital and Royal Victoria Hospital Newcastle on Tyne	1933-1937	7329	4.07
1939	Smith <sup>30</sup>	St. Luke's Hospital N Y	1929-1937	793	3.2
1940	Bower <sup>6</sup>	Philadelphia Hospitals Pa	1928-1937	22,873	4.15
1940	Morse and Rader <sup>32</sup>	Jewish Hospital Brooklyn N Y	1915-1934	8727	2.15
1940	Reid and Montanus <sup>42</sup>	Cincinnati General Hospital Ohio	1934-1938	921	5.97
1940	Stafford and Sprong <sup>32</sup>	Johns Hopkins Hospital Md	1931-1939	1317	3.6
1940	Young <sup>59</sup>	Anderson City Hospital South Carolina	1923-1939	3611	3.04
1941	Aud <sup>3</sup>	Nine Louisville Hospitals Kentucky	1939	1161	3.9
1941	Boyce and Nelson <sup>8</sup>	Charity Hospital La	1930-1941	4963	5.1
1941	Nassau, Lorry and Pulaski <sup>37</sup>	Frankford Hospital Pa	1904-1939	3450	4.2
1941	Rumbold <sup>44</sup>	Genesee Hospital N Y	1925-1939	2013	3.3
1942	Cutler and Hoerr <sup>15</sup>	Peter Bent Brigham Hospital Mass	1913-1940	2192	4.4
1942	Jennings, Burger and Jacob <sup>24</sup>	Beth El Hospital Brooklyn N Y	1930-1938	1680	1.9
1942	Rogers and Faxon <sup>43</sup>	Mass General Hospital Mass	1929-1940	3301	3.06
1942	Slattery and Hinton <sup>49</sup>	Bellevue Hospital (IV Div.) N Y	1928-1939	677	5.1
1943	Hathaway and Watkins <sup>22</sup>	Cleveland Survey Ohio	1930-1942	19,401	4.8
1945	Aycock and Farris <sup>5</sup>	Baltimore City Hospitals Md	1935-1944	1151	3.0
1945	Mueller <sup>33</sup>	Roosevelt Hospital N Y	1935-1944	1481	1.6
1946	Tashiro and Zinniger <sup>54</sup>	Cincinnati General Hospital Ohio	1939-1943	865	3.46

the lowest rate of 0.43 per cent. There was only one death in 1943 and 1945. In the progressive five-year average curve (Fig. 2) the diminution in mortality rate is clearly shown and, during the last five year period, the rate was 1.37 per cent.

These figures compare rather favorably with those reported in other teaching centers, or hospitals with large staffs, and a few of them are listed in Table I.

#### SIMPLE ACUTE APPENDICITIS

Slightly over half our total number belong in this category (2,855 cases) and, perhaps in time, we may eventually witness the vast majority of cases

# ACUTE APPENDICITIS

classified here. There were 14 deaths resulting in a fatality rate of 0.49 per cent. Figure 3 shows the annual mortality rate, and it will be noted that it has been zero during the past six years except for 1944 which discloses the highest annual rate in the period under study, being slightly greater than those recorded in 1920, 1922 and 1924. There were three deaths in 1944. The progressive five-year average is shown in Figure 4 and reveals a fairly uniform curve. For the past five years the rate was 0.39 per cent. Comparable results in other institutions are listed in Table II.

During the latest five-year period there were three deaths in this group, all occurring in 1944. All three were obese and elderly (69, 73 and 76 years of age). The histories were fairly typical and of short duration, but one was

TABLE II

MORTALITY RATES FROM SIMPLE ACUTE APPENDICITIS, REPORTED IN LITERATURE

Year of Publication	Author	Place	Period Studied	No of Cases	Mortality per cent
1940	Barrow and Ochsner <sup>4</sup>	Charity Hospital La	1937-1938	860	0.8
1940	Muller <sup>35</sup>	Iankanau Jefferson and Misericordia Hospitals Pa	1937-1938	259	0.0
1940	Stafford and Sprong <sup>57</sup>	Johns Hopkins Hospital Md	1931-1939	838	0.0
1941	Burke and Kuhn <sup>10</sup>	Municipal Hospital Buffalo, N Y	1935-1946	320	0.58
1941	Haggard and Kirtley <sup>19</sup>	Haggard Clinic, Tenn	1915-1938	2007	0.54
1941	Nassau Lorry and Pulaski <sup>37</sup>	Frankford Hospital Pa	1904-1939	1800	0.44
1941	Rumbold <sup>44</sup>	Genesee Hospital N Y	1925-1939	1499	0.6
1942	Cutler and Hoerr <sup>15</sup>	Peter Bent Brigham Hospital, Mass	1913-1940	1605	1.2
1942	Rogers and Faxon <sup>43</sup>	Mass General Hospital, Mass	1929-1940	2630	0.53
1942	Slattery and Hinton <sup>49</sup>	Bellevue Hospital (IV Div), N Y C	1928-1939	474	1.6
1945	Aycock and Farris <sup>3</sup>	Baltimore City Hospitals Md	1935-1944	895	0.0
1946	Meyer, Requarth and Kozoll <sup>31</sup>	Cook County Hospital, Ill	1944-1945	281	0.78

observed for 48 hours on the medical service, having been admitted ten days previously for hypertension and cardiac insufficiency. The McBurney incision was used in all, and technical difficulties were encountered in one because of a high cecum. All were drained and sulfanilamide was applied locally in two. One patient expired the following day from cardiac failure, pulmonary edema and pneumonia. Another died on the tenth postoperative day from pulmonary infarct and pneumonia, in spite of early ambulation. The third death came on the 14th day, from progressive heart failure and pneumonia. The important contributory factors in this group of deaths were age, obesity and severe cardiovascular and respiratory disturbances. One patient presented a somewhat atypical history and technical difficulties at operation were encountered in another. The appendiceal disease was certainly not the direct cause of death although it was undoubtedly the inciting one.

## ACUTE APPENDICITIS WITH ACUTE LOCAL PERITONITIS

In this group we find almost one quarter (23 per cent) of the total number of our series. There were 26 deaths in the 1,262 recorded cases, resulting in a mortality rate of 2.06 per cent—four times greater than the previous group.

FIG 3

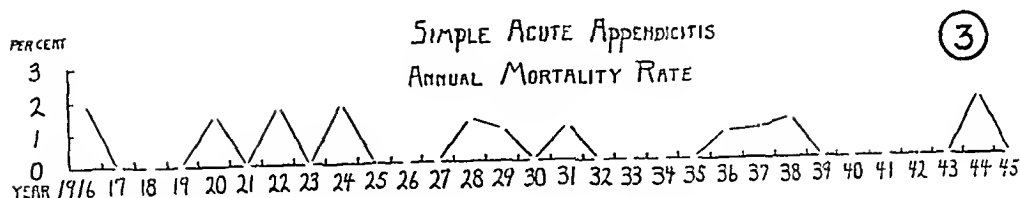


FIG 4

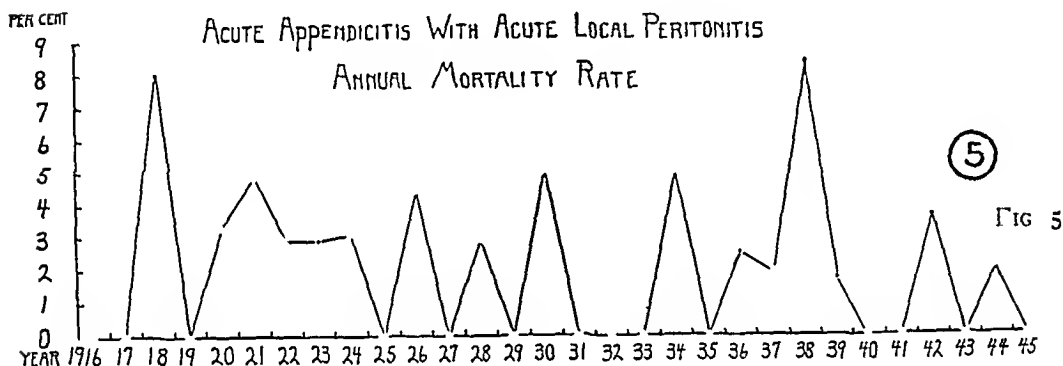
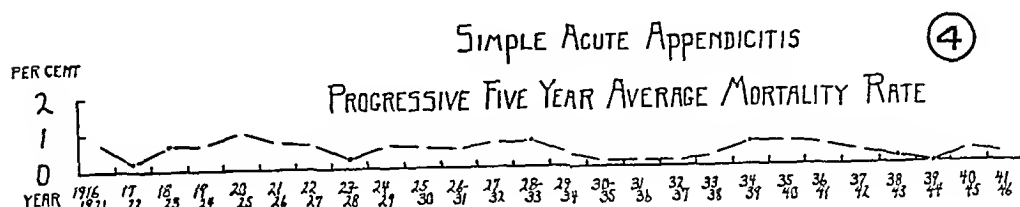


FIG 5

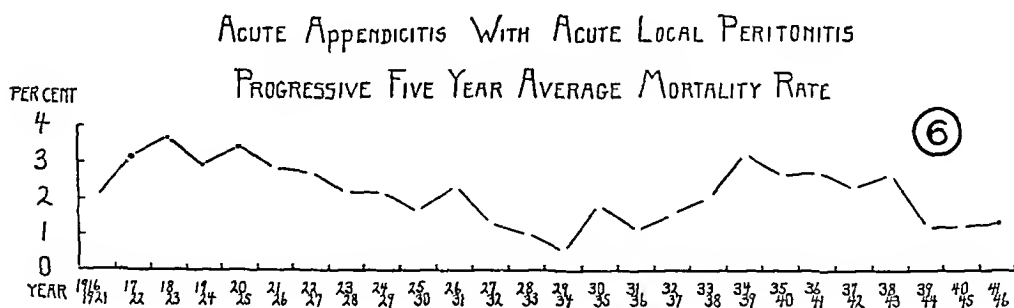


FIG 6

FIG 3—Graph showing annual death rate from 1916 to 1945, inclusive, in 2855 cases of simple acute appendicitis. Total number of deaths 14. Mortality rate, 0.49 per cent. No deaths in 1945.

FIG 4—Graph for comparison with that in Figure 3, showing the progressive five-year average death rate from 1916 to 1945, inclusive, in all cases of simple acute appendicitis. Mortality rate for 1941 to 1946 was 0.39 per cent.

FIG 5—Graph showing the annual death rate from 1916 to 1945, inclusive, in 1262 cases of acute appendicitis with acute local peritonitis. Total number of deaths 26, mortality rate, 2.06 per cent. No deaths in 1945.

FIG 6—Graph for comparison with that in Figure 5, showing the progressive five-year average death rate from 1916 to 1945, inclusive, in all cases of acute appendicitis with acute local peritonitis. Mortality rate for 1941 to 1946 was 1.35 per cent.

The annual death rate fluctuated from 8 per cent to zero (Fig 5) and the last five-year period carried a 1.35 per cent mortality rate (Fig 6). The progressive five-year average shows but little improvement although there was a rather steady decline from the 1916-1921 to the 1929-1934 periods. Since then the curve has shown a serious upward trend and, although the last three periods are not as high as the preceding ones, nevertheless they reveal a slight increase. We are disturbed by these findings, and in examining the records, some of the reasons can be found. The seriousness of the true pathology was often misjudged. There were errors in operative technique. In numerous instances the operator was uncertain whether to drain, or not, and it was obvious he was confused by such pernicious catch phrases as "when in

TABLE III

MORTALITY RATES FROM ACUTE APPENDICITIS WITH ACUTE LOCAL PERITONITIS REPORTED IN LITERATURE

Year of Publication	Author	Place	Period Studied	No of Cases	Mortality per cent
1940	Muller <sup>15</sup>	Lankenau, Jefferson and Misericordia Hospitals Pa	1937-1938	78	1.3
1941	Burke and Kuhn <sup>16</sup>	Municipal Hospital Buffalo New York	1935-1940	44	11.3
1941	Bohmansson and Norup <sup>6</sup>	Orebro Hospital, Sweden	1929-1940	416	11.0
1941	Nassau, Lorry and Pulaski <sup>17</sup>	Frankford Hospital Pa	1904-1939	1159	3.5
1941	Rumbold <sup>14</sup>	Genesee Hospital N Y	1925-1939	239	7.1
1942	Slattery and Hinton <sup>18</sup>	Bellevue Hospital (IV Div) N Y C	1928-1939	67	5.9
1945	Aycock and Farris <sup>3</sup>	Baltimore City Hospitals Md	1935-1944	82	1.2

doubt, drain" or "when in doubt, don't drain." It was evident, too, that some of the residents and younger surgeons were not quite sufficiently knowledgeable in exercising correct judgment in the more difficult cases. Measures to improve such situations will be presented later under "Suggestions for reducing the mortality." Table III illustrates mortality figures in some of the other hospitals in this particular type of appendicitis.

There were three deaths in this group during the last five-year period. The ages were 3, 48 and 57, and the latter two were obese. Only one presented a typical history, another had chills and fever with no localization of pain, and the child complained of sore throat, cough and emesis, followed only later by abdominal cramps. The McBurney incision was used in all. The appendix was gangrenous in each instance and was grossly perforated in two. These two were drained. All received local sulfonamides and two were given parenteral administration in addition. The immediate postoperative course was stormy in all, with marked distention, requiring Miller-Abbott decompression. Type III pneumonia was the cause of death on the 5th day in the case of the child. The second patient also died on the 5th day from pyelophlebitis and bacteremia, and the third case succumbed on the 10th day from massive embolism. Autopsies were obtained on the two adults. The chief contributory factors in causing death were obesity, difficulty in diagnosis, distention, a silent

phlebothrombosis, and existing upper respiratory infection in the case of the child Distention is certainly one of the important predisposing causes of thrombosis, with its threat of infarction or embolism Fever and chills were ominous symptoms in the patient dying from pylephlebitis and sepsis, but such symptoms do not necessarily presage a fatal outcome

FIG 7

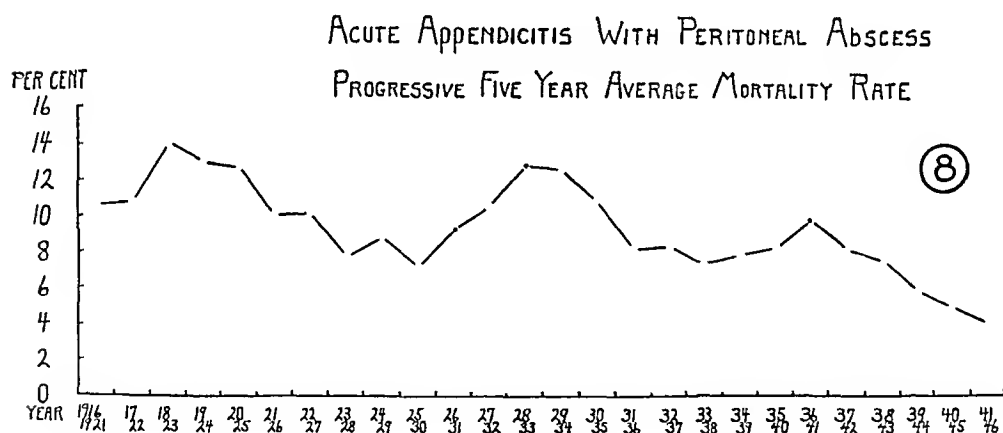
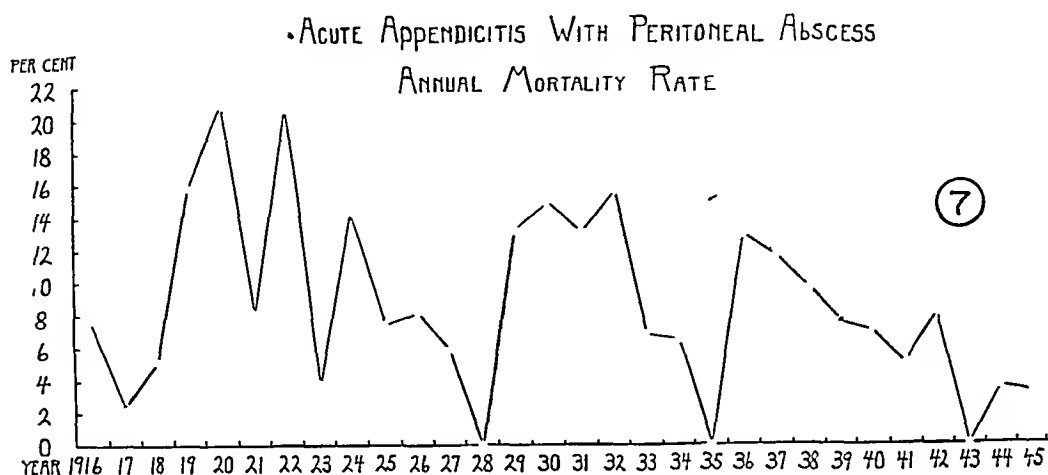


FIG 8

FIG 7—Graph showing the annual death rate from 1916 to 1945, inclusive, in 896 cases of acute appendicitis with peritoneal abscess Total number of deaths 81, mortality rate, 9.04 per cent Mortality rate for 1945 was 3.45 per cent

FIG 8—Graph for comparison with that in Figure 7, showing the progressive five-year average death rate from 1916 to 1945, inclusive, in all cases of acute appendicitis with peritoneal abscess Mortality rate for 1941 to 1946 was 4.16 per cent

#### ACUTE APPENDICITIS WITH PERITONEAL ABSCESS

There were 896 cases of primary appendiceal abscess, this comprising 16 per cent of the whole series The 81 deaths in this subgroup produce a mortality of 9.04 per cent In Figure 7 one notes a high rate of 20 per cent in

1920 and 1922 while in 1928, 1935 and 1943 it was zero. The last year of the present study shows a mortality rate of 3.45 per cent. The progressive five-year average (Fig. 8) reveals a steady decline since the 1936-1941 period, and the last five-year interval registers a mortality of 4.16 per cent, a little less than half the total rate for this group. Our results are therefore encouraging.

In Table IV comparable rates from other hospitals are shown, but does not include any series treated conservatively or by delayed methods of therapy.

There were four deaths from appendiceal abscess in the last five-year period. Three patients were elderly (60, 71 and 78) and obese. The fourth patient was 36. Severe hypertension was observed in the 60-year-old patient. The duration of illness was two days, five days (in two), and two weeks. Only one presented a typical history, but it was suggestive in another. Two took

TABLE IV

MORTALITY RATES FROM ACUTE APPENDICITIS WITH APPENDICEAL ABSCESS REPORTED IN LITERATURE

Year of Publication	Author	Place	Period Studied	No. of Cases	Mortality per cent
1940	Boyce <sup>7</sup>	Charity Hospital La	1930-1939	323	10.8
1940	Reid and Montanus <sup>42</sup>	Cincinnati General Hospital Ohio	1934-1938	129	10.0
1940	Stafford and Sprong <sup>51</sup>	Johns Hopkins Hospital Md	1931-1939	283	7.06
1941	Nassau, Lorry and Pulaski <sup>37</sup>	Frankford Hospital Pa	1904-1939	135	8.8
1941	Rumbold <sup>44</sup>	Genesee Hospital N Y	1925-1939	130	18.4
1942	Cutler and Hoerr <sup>15</sup>	Peter Bent Brigham Hospital Mass	1913-1940	247	7.3
1942	Slattery and Hinton <sup>49</sup>	Bellevue Hospital (IV Div.), N Y C	1928-1939	88	7.9
1942	Stafford <sup>51</sup>	Johns Hopkins Hospital Md	1939-1941	42	2.38
1943	Budd and Watkins <sup>4</sup>	Cleveland Survey Ohio	1940-1941	113	9.7
1945	Aycock and Farris <sup>3</sup>	Baltimore City Hospitals Md	1935-1944	58	6.9

cathartics. One patient was observed for a week after admission and another underwent decompression with a Miller-Abbott tube for several days before operation. The McBurney incision was employed in three, but a left rectus was chosen in the fourth because this was the most prominent region of the abscess. Twice the surgeon encountered serious technical difficulties. The appendix was not removed in two others. Spinal anesthesia was administered twice and nitrous oxide-ether was chosen for the other two. Sulfonamides were introduced locally in two, but all received parenteral sulfa therapy. Penicillin was used, in addition, for one patient. The immediate postoperative reaction was quite satisfactory in three, but one developed moderate distention on the following day. One patient (with hypertension) died on the second day from massive pulmonary embolism and acute pulmonary edema. Another succumbed on the 5th day from paralytic ileus and type VI pneumonia. There was also a question of a flare-up of a quiescent pulmonary tuberculosis. Neither of these cases were autopsied. The third patient (with incision and drainage of appendiceal abscess only) had a smooth postoperative course and was allowed up on the 11th day. Six days later he went into sudden collapse and died. Autopsy revealed a large saddle embolus at the bifurcation of the

pulmonary artery There was a bilateral phlebothrombosis of the external iliac and femoral veins The peritoneum was clean except for the region of the appendiceal abscess The appendix was laterocecal with a perforation 5 cm from the base There was no clinical evidence of thrombosis during the postoperative period The fourth patient (watched for one week after admission, incision and drainage of appendiceal abscess only) suffered a long difficult postoperative course A secondary intraperitoneal abscess was incised and drained ten days after operation Six days later he revealed a pneumonitis in the right lower lobe On the 26th day, there was evidence of a pyelephlebitis, followed by incision and drainage of a left subphrenic abscess on the 40th postoperative day This required revision in another ten days Blood culture

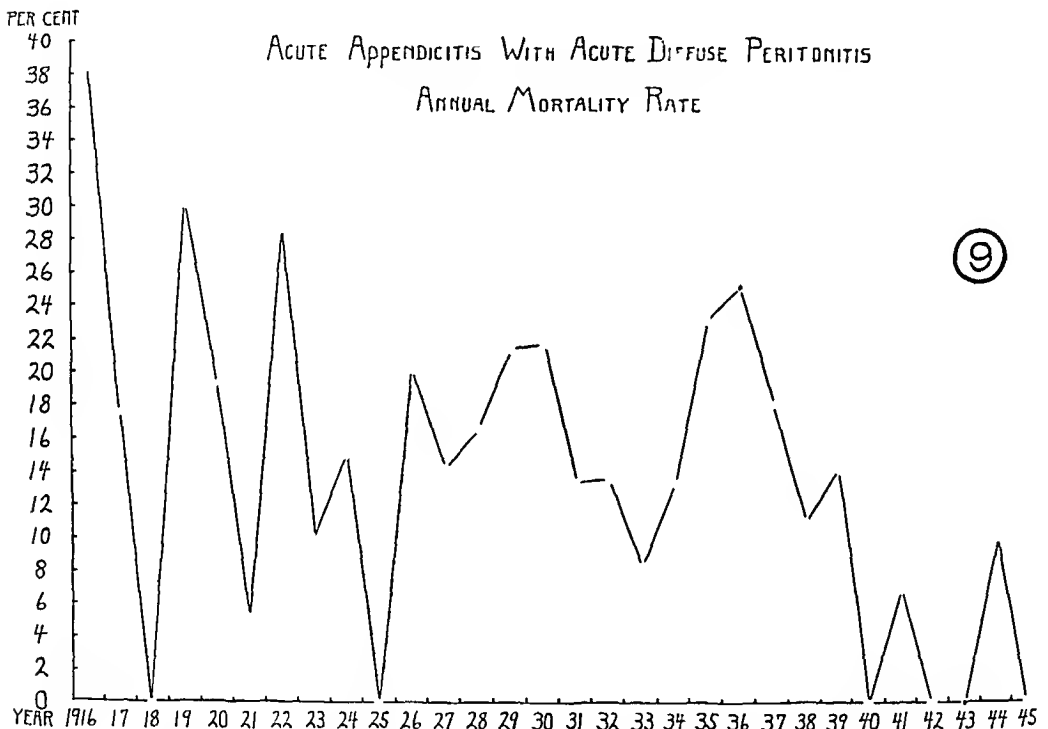


FIG 9—Graph showing the annual death rate from 1916 to 1945, inclusive, in 452 cases of acute appendicitis with acute diffuse peritonitis Total number of deaths 70, mortality rate 15.48 per cent No deaths in 1945

on the 45th day disclosed a non-hemolytic streptococcus A left suppurative pleurisy then developed which required drainage on the 52nd day He continued to worsen, his general sepsis could not be controlled, and he expired on the 90th postoperative day from bacteremia, pyelephlebitis, meningitis or metastatic cerebral abscesses No autopsy was obtained

The chief factors in these four deaths were advanced age in three, obesity in two, hypertension in one, unrecognized diagnosis in two, and failure to appreciate a postoperative bilateral femoral phlebothrombosis

ACUTE APPENDICITIS

ACUTE APPENDICITIS WITH ACUTE DIFFUSE PERITONITIS

Four hundred fifty-two cases, 834 per cent of the total number, revealed a diffuse, or spreading peritonitis, at the time of operation. There were 70 deaths, producing a mortality rate of 15.48 per cent. Figure 9 illustrates the annual mortality rate and during the first 20 years the rate was quite high, although there were two years (1918 and 1925) without any deaths. In the past nine years there has been a marked diminution in the

TABLE V

MORTALITY RATES FROM ACUTE APPENDICITIS WITH ACUTE DIFFUSE PERITONITIS REPORTED IN LITERATURE					
Year of Publication	Author	Place	Period Studied	No of Cases	Mortality per cent
1941	Nassau Lorry and Pulaski <sup>37</sup>	Frankford Hospital, Pa	1904-1939	356	23.6
1941	Rumbold <sup>44</sup>	Genesee Hospital, N. Y.	1925-1939	145	18.0
1942	Slattery and Hinton <sup>49</sup>	Bellevue Hospital (IV Div.) N. Y. C.	1928-1939	48	33.3
1945	Aycock and Farris <sup>5</sup>	Baltimore City Hospitals Md	1935-1944	116	25.0

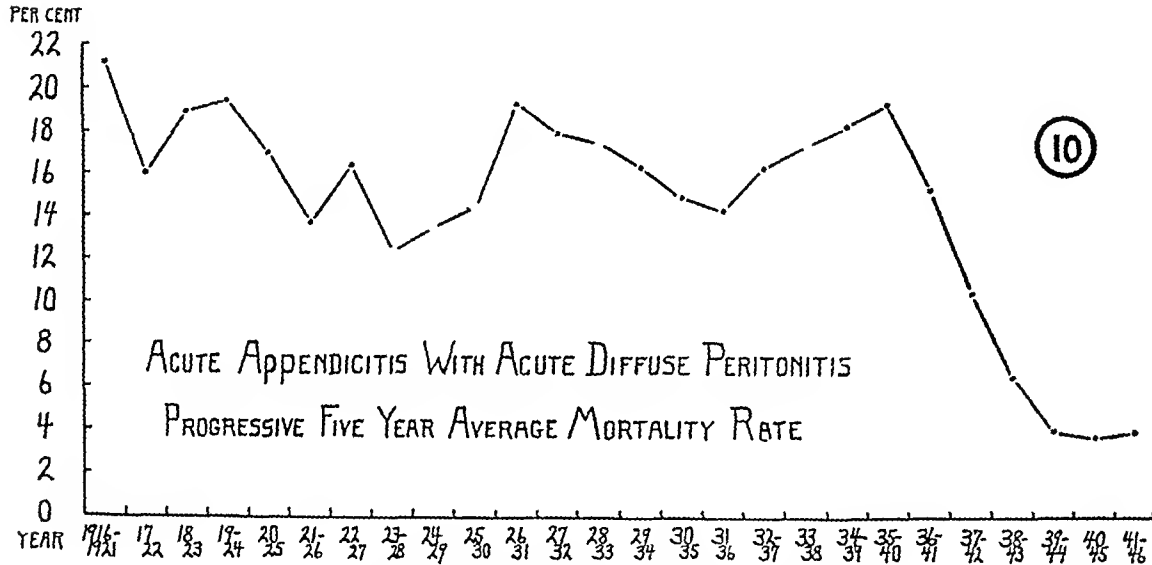


FIG 10—Graph for comparison with that in Figure 9, showing the progressive five-year average death rate, from 1916 to 1945, inclusive, in all cases of acute appendicitis with acute diffuse peritonitis. Mortality rate for 1941 to 1946 was 4.08 per cent.

death rate, and no fatalities took place in 1940, 1942, 1943 and 1945. The progressive five-year average (Fig 10) illustrates this rather strikingly, particularly from the 1936-1941 period to the latest one (1941-1946) which registered a mortality rate of 4.08 per cent.

Table V illustrates comparable figures in other hospitals but excludes results obtained from conservative or delayed operative treatment.

Two deaths are recorded in the past five years. One was 54 and the other was 82 years old. Both were thin. The former had a one day atypical, and the latter a two day typical history. There was marked hypertension and cardiac enlargement in the elder one. The diagnosis in the younger patient



was perforated peptic ulcer, so that an upper right rectus incision was made. It was necessary to extend it caudad. The appendix was lateroretro cecal, with a perforation near the base. There was no evidence of a localizing process. He took the anesthesia very poorly and it was necessary to resort to open ether. Culture of the pus revealed five organisms, indicating the severity of the infection. A McBurney incision with local anesthesia was chosen for the elder patient. A meso-cecal gangrenous appendix was found with a perforation at the middle third. Thin odorless pus was welling in from all sides of the operative field. The culture grew out a non-hemolytic *b. coli*. Five grams of sulfanilamide were placed into the operative field. Removal was technically difficult. The immediate postoperative reaction was rather severe in both patients. They received parenteral sulfa therapy, and penicillin was administered to the younger patient, in addition. He also required decompression with the Miller-Abbott tube. Bilateral pneumonia developed over both bases at the end of 24 hours and he died of shock and overwhelming infection 50 hours after operation. No autopsy was obtained. The elder patient responded rather well during the first postoperative week. She then incurred bilateral pneumonia in the second week. During the following week there was evidence of cul-de-sac abscess, and this ruptured spontaneously per vagina. For some unexplained reason, a rectovaginal fistula developed in the fourth week and on the 28th postoperative day there was a sudden severe hemorrhage from the abscess and fistula site, and she died soon after. Autopsy showed a clean peritoneum, a small residual abscess in the left lower quadrant, and the cul-de-sac abscess communicating with the rectovaginal fistula. No specific bleeding point was found.

The important factors which played a role in these two deaths were age, atypical history, wrong preoperative diagnosis, hypertension, misplaced incision, poorly tolerated anesthetic, technical difficulty at operation, pneumonia, overwhelming polybacterial infection, and a severe fatal hemorrhage.

#### ACUTE APPENDICITIS WITH ACUTE PROGRESSIVE FIBRINOPURULENT PERITONITIS

Fortunately there were only 34 such cases in the present series, or 0.6 per cent. All but six died. The death rate is therefore very high, namely 82.35 per cent. There was only one survival amongst the five cases during the last five-year period.

The four deaths are briefly presented. They were in the middle age group, ranging from 37 to 53. The sexes were equally divided. The duration of illness ranged from two to ten days. Three were obese. All presented atypical histories. One patient (age 53) was diagnosed as renal colic. Twenty-four hours later the diagnosis was changed to acute cholecystitis. Six hours later he was taken to the operating room with a diagnosis of gangrenous cholecystitis with perforation. Two incisions were made: a paracostal over the gall-bladder and then a McBurney incision with drainage of an appendiceal abscess. He died in the operating room just as the dressings were applied. Autopsy revealed a fibrinopurulent peritonitis, a retrolatero cecal abscess,

with a gangrenous perforated appendix fixed to the posterior cecal wall. Culture of the peritoneal pus grew out a *b. coli*.

The second patient (age 51) was admitted in shock, with a diagnosis of perforated peptic ulcer, having acknowledged a 24-year ulcer history. In spite of supportive treatment, he never recovered from shock and died soon after admission. Autopsy showed a generalized fibrinopurulent peritonitis, a perforated gangrenous appendix lying in the pelvis and a healed duodenal ulcer.

The third patient (age 42) was thought to have an acute ileus secondary to adhesions from radiotherapy, or to recurrence of an ovarian carcinoma. Because the maximum signs presented in the left lower quadrant, a left lower rectus incision was made under local anesthesia. A fibrinopurulent peritonitis was encountered and, because of the patient's precarious condition, no further exploration was made. She died six hours after operation. Autopsy disclosed a generalized fibrinopurulent peritonitis, a large abscess behind the terminal ileum and cecum extending to the sigmoid on the left and to a pelvic mass below. A perforated necrotic appendix extended into the abscess.

The last patient (age 37) was admitted with a diagnosis of acute cholecystitis and only after 24 hours' observation was the true nature of the disease process suspected. Through a McBurney incision, a high retrocecal and retrocolic gangrenous perforated appendix was found. The surgeon experienced considerable technical difficulty in the procedure and it was hard to control bleeding. There was a generalized fibrinopurulent peritonitis in addition. In spite of local and parenteral sulfonamide therapy, transfusions, and decompression with the Miller-Abbott tube, she had a very stormy course and died on the third postoperative day. A blood culture was sterile. Peritoneal culture grew out a *b. aerogenes*. At autopsy there was a widespread fibrinopurulent peritonitis. A culture of the heart's blood revealed an anaerobic green streptococcus.

The chief factors in the mortality amongst these four cases are: Wrong diagnosis, resulting in serious delay in two instances, obesity in three, two incisions in one case, serious technical difficulties with bleeding in another, and general sepsis, collapse, and shock in all of them.

Figure 11 reveals the progressive five-year average curves for all cases of acute appendicitis (curve V), together with the various subgroups, excepting acute appendicitis with generalized fibrinopurulent peritonitis. These curves therefore reflect their relationship, one to another, and reveal the general mortality trends over the period of time under study. As already noted, there has been a definite rise in mortality from acute appendicitis with acute local peritonitis and our chief concern, therefore, is directed to this subgroup.

Table VI illustrates the mortality rate for all cases of acute appendicitis, as well as each of its subgroups, for the 30-year span, also the most recent five-year period, and the last year of the study. It is gratifying to note that the mortality rates in the middle column are very much better than those in the first column, whilst those in the right hand column are even lower than

those shown in the middle one. Attention is also directed to column one where the mortality rate quadruples with spread of the disease in the earlier phases. It nearly doubles in rate between abscess and diffuse peritonitis, and then increases almost sixfold between acute diffuse peritonitis and fibrinopurulent peritonitis.

## GENERAL REMARKS

The diminution in our appendicitis fatalities is in keeping with similar reports from other hospitals and clinics. In fact, a marked reduction has taken place throughout the nation since 1930. In that year the mortality was 15.3 per 100,000 whilst in 1945 the rate was 5.1 per 100,000,<sup>78</sup> or 6,697 deaths

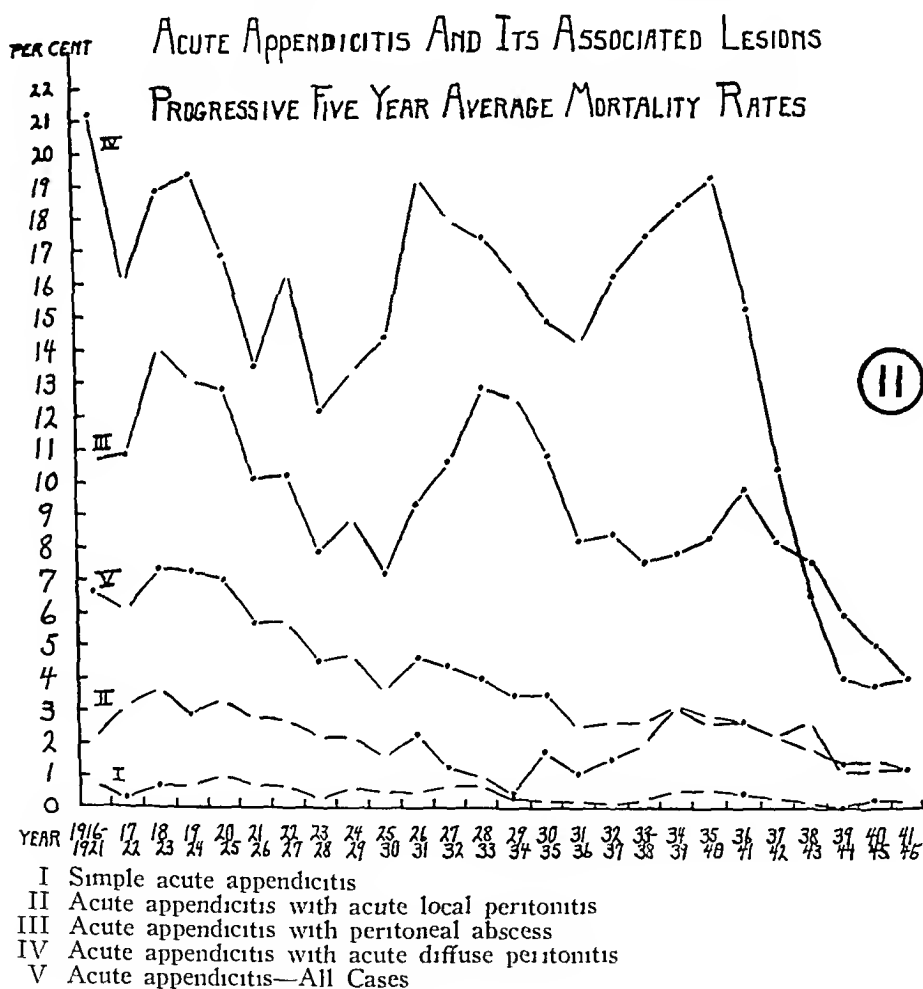


FIG. 11.—Graph showing the progressive five-year average mortality curve from 1916 to 1945, inclusive, for all cases of acute appendicitis and its associated lesions (curve V) as well as its various subgroups (curves I to IV) with the exception of subgroup comprising acute appendicitis with progressive generalized fibrinopurulent peritonitis.

With so little value placed on human life in recent years, this death rate is small indeed, yet it seems that we really should exert our every effort to reduce it further.

# ACUTE APPENDICITIS

There are numerous reasons for this nationwide reduction in appendicitis deaths. The coordinated plans on the part of the public health service combined with the sponsorship of local medical societies, industries, insurance companies, schools, universities, and municipal authorities have served to render the laity conscious of two serious dangers of appendicitis, namely, delay and purgation. In our own series we find that there is a slight but definite reduction of our peritonitis cases, even though our annual incidence of acute appendicitis remains about the same. This suggests that the population in our area has become appendicitis conscious, or that the physicians, serving this region, are recognizing and diagnosing the disease process early and promptly.

Another factor in reducing appendicitis mortality has been the more thorough teaching and training of our residents. During our most recent five-year period, there were more deaths incurred by the attending than by the resident staff.

TABLE VI  
ACUTE APPENDICITIS AT THE PRESBYTERIAN HOSPITAL, NEW YORK CITY  
January 1, 1916 to December 31, 1945

Classification	Mortality Rate 1916-1945	Last Five Year Average Mortality Rate	1945 Mortality Rate
All cases of acute appendicitis	3.55%	1.37%	0.43%
Simple acute appendicitis	0.49%	0.39%	0.00%
Acute appendicitis with acute local peritonitis	2.06%	1.35%	0.00%
Acute appendicitis with peritoneal (appendiceal) abscess	9.04%	4.16%	3.45%
Acute appendicitis with acute diffuse peritonitis	15.48%	4.08%	0.00%
Acute appendicitis with progressive fibrinopurulent peritonitis	82.35%	80.00%	*0.00%
* No cases for 1945			

The past decade has witnessed great advances in the care and treatment of the sicker type of patient, for instance, preoperative preparation, appreciation of fluid balance requirements, deficiency states such as anemia and hypoproteinemia, more liberal use of plasma, blood, and oxygen therapy, gastrointestinal decompression, means of anticipating and controlling thrombophlebitis with its threat of infarction or embolism, and early ambulation. Of great importance has been the marked advance in methods of anesthesia and in its skillful administration. The advantage of utilizing the services of a highly trained staff of well trained and resourceful anesthetists is obvious. In close association with the latter, there has been a steady improvement in operative technic, with fewer technical errors and blunders, together with the more frequent use of the McBurney incision.

A further factor in the diminution of appendicitis fatalities has been the advent of the antibacterial agents. The role of the sulfonamides is known to all, and everyone is familiar with the reports of Ravdin, Lockwood and Rhoads,<sup>40</sup> Harvey, Meleney, and Rennie,<sup>21</sup> Mueller and Thompson,<sup>34</sup> Jackson and Collier,<sup>23</sup> Thompson, Brabson and Walker,<sup>55</sup> Stafford,<sup>51</sup> Chesterman,<sup>11</sup> Aycock and Faris<sup>3</sup> and numerous other observers. We have not employed it

consistently or set down any rigid rules with reference to its use, but prefer to leave the decision with the surgeon, who will base his judgment on the merits of any given case. The writer is disposed to use it locally and systemically in patients with local or widespread peritonitis, and to employ it parenterally in cases of appendiceal abscess. The more recent reports of Altemeier,<sup>1</sup> Crile,<sup>12, 13</sup> Crile and Fulton,<sup>14</sup> Fauley and his associates,<sup>16</sup> and others, suggest that large doses of penicillin probably inhibit the escherichia organisms and may be beneficial in polybacterial peritonitis of appendiceal origin. The results of the last two groups of investigators may necessitate a change in our present policy of treating appendiceal abscess and spreading appendiceal peritonitis. Perhaps, in the discussion, Doctor Lockwood will relate his interpretation of the mechanism and mode of action of penicillin on the gram negative intestinal bacilli in connection with appendiceal peritonitis. We have used penicillin, both alone and in conjunction with the sulfonamides, but we have not a sufficient number of cases on which to base any conclusions. The use of streptomycin in appendicitis with peritonitis or abscess is still speculative, but a preliminary report on experimental peritonitis in dogs by Zintel and his associates<sup>60</sup> suggests that it is not as helpful as the combined effect of penicillin and the sulfonamides.

We are also impressed by the causes of death during the last five-year period of our study, in that our improved methods of therapy appear to have diminished the fatalities from peritonitis, general sepsis, pneumonia and embolism. The chief factors in our recent deaths are: Advanced age, hypertensive cardio-vascular disease, obesity, diabetes, atypical history, wrong diagnosis, and technical errors such as misplaced incisions, difficulty in removing the appendix, and lack of understanding the indications for drainage. Other factors were improper choice of anesthetic, failure to recognize a latent thrombophlebitis and inability to control distention.

One must not neglect to pay tribute to the greatly depleted attending staff, and the resident and assistant resident surgeons, with their accelerated and shortened training period, who, during the war years, continued to maintain a low mortality record at this hospital (Fig 1).

Thus there are many factors responsible for the lowered mortality rate of acute appendicitis but perhaps the most important of all are the sober judgment, skill, and experience of the surgeon combined with his observance of fundamental precepts and sound surgical principles.

#### SOME PRACTICAL CONSIDERATIONS

Our general policy has been one of prompt operation, and we fully concur with the arguments, for early surgical intervention, as set forth by Stone,<sup>53</sup> Ogilvie,<sup>39</sup> Stafford and Sprong,<sup>52</sup> Gile and Bowler,<sup>18</sup> Maes and his associates,<sup>30</sup> Shipley,<sup>47, 48</sup> Thornton,<sup>56</sup> Nichols,<sup>38</sup> Mueller,<sup>33</sup> Lahey,<sup>27</sup> Scott and Ware,<sup>46</sup> and numerous others. When necessary, our patients may undergo several hours of preparation before operation, including resuscitative measures and restoration of fluid balance. This form of therapy is not to be construed as "delayed"

treatment in the sense employed by the more conservative school of surgeons

The type of anesthetic should be chosen by the anesthetist, after due appraisal of the case with the surgeon in charge. This tends to minimize the danger of routine and rule of thumb methods. The writer is disposed to favor spinal anesthesia, whenever it is considered safe, because of complete wound relaxation and relatively greater ease in exposing the site of pathology without undue retractor trauma. However, there are numerous occasions when a patient's condition does not permit the use of spinal anesthesia and, in such instances, we resort to some other anesthetic agent. As Rogers and Faxon<sup>43</sup> have indicated, the operation should not exceed an hour. There are rare exceptions to this. Speed is desirable at times but never at the expense of technical precision and gentleness to the tissues.

The McBurney incision is extensively employed at this institution, but if circumstances indicate the advisability of another approach, we do not hesitate to do so. Doctor Whipple has repeatedly stated "Fit the incision to the patient, not the patient to the incision." A liberal incision is desirable and, if technical difficulties are encountered in satisfactorily demonstrating our surgical objective, the incision should be enlarged—caudad by Weir extension, or, if necessary, division of the outer portion of rectus muscle and sheath,—cephalad by transecting the internal oblique and transversus abdominis muscles.

The intelligent use of retractors is often overlooked, resulting in unnecessary roughness and trauma to the wound. Since most of these wounds are contaminated by reason of the infected appendix, the danger of intramural infection becomes increasingly greater by overzealous retraction on the part of the second assistant. Retractors should be inserted and placed with great care and exactness, and the operator should frequently admonish his assistant to exert minimal force consistent with adequate exposure.

The appendix should be sought with extremely careful manipulation and maneuvers, and with the least possible disturbance of the surrounding viscera. It may be necessary, at times, to divide the lateral peritoneal reflection of the cecum in order to mobilize a high retrocolic appendix. Division of a thick, friable, edematous mesoappendix must be executed with the greatest care and gentleness because, if this structure tears, the blood vessels retract, and often-times it is almost impossible to control the resultant bleeding. We prefer to invert the appendix stump but simple ligation is quite proper, particularly when the adjacent cecal wall is thickened and friable. We strongly condemn combined ligation and inversion of any appendix stump.

If it is decided to drain (*vide infra*) a case of local peritonitis, it is better to insert one or two simple Penrose or cigarette drains. These should be removed relatively early, depending, of course, on the general condition of the patient, the temperature curve, the amount and character of the discharge, the bacteriology of the pus, and the region and anatomical peculiarities of the area drained. For primary appendiceal abscess, it is preferable to introduce a tampon, with gauze packs or cigarette drains placed within it. This permits

free drainage, keeps the wound well "sprung," thus preventing narrowing or "bottle necking" of the superficial portion of the tract, and, lastly, encourages healing from within out, by arresting premature infolding of the adjacent intraperitoneal structures. Sometimes we introduce a small soft rubber tube or catheter along the lateral aspect of the tampon for purpose of subsequent irrigations. In any event, it is extremely important *never* to insert a drain *across* a viscus if it can possibly be avoided. This is one of many reasons for choosing the McBurney incision because it lends itself so well in the proper placement of drains.

If, in the removal of an unperforated gangrenous appendix, the surgeon decides against intraperitoneal drainage, it is wise to insert a small drain to the muscle or properitoneal layer, because such wounds are almost certainly heavily contaminated. No possible harm can come from this, and the surgeon enlists an added factor of safety for his patient. Elderly, obese and diabetic individuals should also receive intramural drainage even though the peritoneum may be closed.

The reader is familiar with present-day methods of postoperative therapy, but there is one point which deserves special emphasis, namely, the desirability of medical teamwork. This is particularly important in connection with older patients. Too often we are inclined to "wait and see," only to call upon our medical consultants when signs of heart failure or pneumonia or apoplexy have already set in. It is far preferable to invite medical council before anything serious has taken place. Such close association between surgeon and internist may forestall many serious complications.

#### INDICATIONS FOR DRAINAGE

For many surgeons, the problem of drainage seems to progress in cycles. In the beginning, one usually starts with a firm resolve to follow the principles governing drainage. In due course of time, a tendency develops to overlook the teachings of medical school and early intern days. As experience increases, the surgeon may discard or revise the precepts of his instructors. This in itself is not reprehensible because progress demands vision and imagination, as well as reflection and deliberation. But sooner or later, a time arrives when boldness and self-confidence will outbalance sound judgment and critique. Then comes the final step—a serious oversight or blunder, resulting in a severe and stormy postoperative course, perhaps in death. At Staff Conference, the case is reported and discussed, the error is recognized and acknowledged. There is the usual expression of remorse and regret, followed by a reaffirmation of the indications for drainage. This marks the beginning of the next cycle, and others to follow. Unfortunately, with the advent of antibacterial agents and better methods of treatment, it is tempting and misleading to overlook sound fundamental principles of surgical therapy.

For teaching purposes, and particularly for interns and residents, and also for younger members of attending surgical staffs, the indications for drainage are herewith presented. They should be observed by surgeons of average

ability, such as Doctor Jones, Doctor Smith, Doctor Brown and myself. To the highly skilled, experienced master surgeon, some of these suggestions will appear superfluous and perhaps even unnecessary.

- Presence of an abscess
- Necrotic or compromised tissue remaining in the operative field
- Inability or inadvisability to remove the focus of infection (appendix)
- Gross contamination from
  - perforation of appendix
  - break in technic
- Extensive exposure of retroperitoneal tissue
- Uncontrolled bleeding
- Insecure ligation or closure of the appendiceal stump
- Severe operative trauma

There are certain corollaries to these rules, such as an extremely difficult technical procedure with retrograde removal of the appendix, also the presence of two or more organisms in the direct smear of the exudate or pus. In addition, there are also some variable factors which may enter into a decision to drain, namely, age, debility, cachexia, obesity, diabetes, and other constitutional diseases. The indications for drainage of the intramural portion of these wounds have already been discussed. If the thoughtful conscientious surgeon will keep these criteria for drainage clearly in mind, he will have no need for untimely and ill conceived catch phrases to misguide or influence his final decision. He can act without fear or misgiving. Application of these principles governing drainage will contribute, in no small measure, to a substantial reduction of deaths, especially in the subgroup of acute appendicitis with local peritonitis. Severe postoperative reactions and serious complications will also diminish in this particular subgroup.

#### SUGGESTIONS FOR FURTHER REDUCTION OF MORTALITY FROM ACUTE APPENDICITIS

The continuation of public education in the dangers of purgation and delay, and in the advantages of early diagnosis and prompt operation, in acute appendicitis, should be vigorously supported by appropriate local, state and national authorities and agencies. The results of such concerted action are already known, and they have contributed greatly toward the reduction of appendicitis deaths in the nation as a whole.

In our institution, we believe a further diminution in mortality can be effected as follows:

- Earlier recognition of atypical cases
- Require the attending surgeon, on call, 1) to examine all cases of uncertain or equivocal diagnosis,
  - 2) to scrub with the resident or assistant resident if the patient
    - a) is obese
    - b) is 45 years or over
    - c) gives a 48-hour history, or longer
    - d) presents a doubtful diagnosis



Careful planning with reference to operative preparation and approach,  
proper choice of anesthesia, and postoperative care  
Anticipation and prevention of complications, particularly thrombo-  
phlebitis, severe distention, and spread of intra-abdominal infection  
Unceasing efforts to improve operative technic  
Recognition of indications for drainage  
Close teamwork with the medical staff in any case presenting potentially  
serious non-surgical complications  
Continued study of experimental peritonitis, particularly along lines  
described by Kay and Lockwood<sup>25, 26</sup>  
Early ambulation in selected cases  
Annual review, at surgical staff conference, of acute appendicitis,  
together with a discussion of complications, methods of treatment,  
death analysis, and suggestions in formulating our policy for the  
ensuing year

#### SUMMARY

A study of the mortality from acute appendicitis, at a University Hospital, covering a period of 30 years, has been presented

There has been a satisfactory progressive over-all reduction in the mortality rate, which is in keeping with reports from other hospitals and in the nation as a whole

The reasons for such a general diminution in appendicitis deaths have been noted

The various subgroups in our series have also shown a substantial decline except for Acute Appendicitis with Acute Local Peritonitis, which disclosed an increased mortality rate. Some of the factors responsible for this rise have been discussed. Suggestions have been submitted to improve and control it.

Appendicitis deaths, during the last five-year period, have been somewhat different from those analyzed in the earlier years of this study. There are proportionately fewer fatalities from intraperitoneal infections and complications, and relatively more from cardiovascular and other nonsurgical conditions.

We have reviewed the indications for drainage and have emphasized a few practical points in operative technic and management of acute appendicitis.

A plan for further improvement of our appendicitis mortality rate has been submitted.

In the light of recent reports and investigations, it may become necessary and advisable to change the present policy of treatment for appendiceal abscess and diffuse peritonitis at this institution.

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DISCUSSION—DR FRIEDRICK A BOTH, Philadelphia The Appendicitis Mortality Committee of the Philadelphia County Medical Society analyzed the deaths from appendicitis in 17 hospitals in Philadelphia during 1944. Our analyses for the years 1945 and 1946 are not completed at this time. Eight of the 17 hospitals were teaching institutions and many of the surgeons in the other nine were connected with a teaching institution. The Philadelphia Department of Public Health cooperated in this study by sending a copy of the death certificates of all patients dying from appendicitis to the Secretary of the Philadelphia County Medical Society. A comprehensive questionnaire was filled out for all deaths.

In the 17 institutions noted above there were 4997 cases of appendicitis operated upon in 1944, 3248 for acute appendicitis without perforation, 1328 for acute appendicitis with perforation and its sequela, and in 421 patients chronic appendicitis was found. We are only a fact-finding committee, however, an analysis of the deaths as they occurred in these 17 hospitals revealed several interesting facts.

In the 4997 cases there were 47 deaths. The time that elapsed between the onset of symptoms and the patient having consulted a physician was less than six hours in 13 instances, six to 24 hours in 15 instances, one or more days in 26 instances and two or more days in 19. We then studied the time that elapsed after the physician was called before the patient was hospitalized. In 28 cases it was less than six hours, in 32 it was less than 24 hours, in 15 it was more than 24 hours and in 12 it is more than three days. We tried to ascertain whether or not a cathartic had been taken before hospitalization. In 22 cases no cathartic was taken, eight patients had given themselves a cathartic and the physician had ordered one in two instances. In 15 cases we were unable to determine whether or not a cathartic was given. The findings at operation showed acute appendicitis in five cases, perforation with generalized peritonitis in 17, perforation with abscess formation in 15, chronic appendicitis in one, normal appendix in one, findings indefinite in three and no operation was performed in five cases.

We noted in four instances that there was a marked delay in obtaining surgical consultation after the patient was admitted to the hospital. These cases had been admitted to the medical service instead of having the benefit of immediate medical and surgical consultation. In one case the surgeon was not called for 12 hours, in two cases not for 24 hours and in one, more than 36 hours. This prompted us to request that all patients hospitalized with abdominal pain should have both surgical and medical consultation immediately upon admission. In an effort to determine whether the person performing the operation contributed to these deaths we studied who had performed the operation. It was found that the attending surgeon operated upon 30 of these patients, the associate on five and the resident on 12.

There were nine deaths in known cardiacs, occurring eight to ten days after the operation. This was rather surprising as we had felt that cardiac cases under the care of a cardiologist prior to surgery would be more likely to succumb in the first 72 hours after operation. There were seven deaths from pulmonary embolism. This again demonstrates the high percentage of patients who died from this serious postoperative complication, and emphasizes the value of a femoral or higher ligation as an aid in preventing its occurrence.

DR ROY D McCURE, Detroit Dr Arthur McGraw, who is unavoidably absent today, was stimulated by Dr Schullinger's abstract to look up our statistics. At Henry Ford Hospital during the ten years from 1937 to 1946, there were 13 deaths following 1405 appendectomies for acute appendicitis, an over-all mortality of 0.92 per cent. In the same year drainage only was performed in 68 cases of appendix abscess with one death, a mortality of 1.5 per cent. During the last five years there has been but one death in 601 appendectomies for acute appendicitis, during the last four years, no deaths in 466 similar appendectomies.

This reduction in mortality cannot be attributable to penicillin because that drug

# ACUTE APPENDICITIS

became available for unrestricted use only in 1946. Though used to some extent, sulfonamides have probably not been a large factor in improved mortality. The Wangenstein principle of gastroduodenal decompression and drainage has been available to us and used through the ten-year period, the Miller-Abbott tube for only a few less years. Both methods, however, have undoubtedly been of greatest help in the most recent years by reason of their more frequent, skillful and therefore effective use. Increasing and more intelligent attention to maintenance of electrolyte, metabolite and water balance has undoubtedly been a large factor. It is interesting to note, however, that the only probably helpful factor virtually restricted to the last five years is early ambulation.

In addition, several points in technic which we have adhered to for the past 25 years may have a favorable influence on appendectomy mortality: (1) Favoring the muscle-splitting incision, (2) identifying the appendix by locating its origin at the convergence of the three longitudinal striae of the cecum rather than by searching for the tip with the index finger, (3) avoidance of "packing off" of the peritoneal cavity, (4) avoidance of drain material any heavier or stiffer than rubber dam.

## BRIEF SUMMARY—HENRY FORD HOSPITAL 13 post-appendectomy deaths

Duration of symptoms—one-half day to 12 days

### Causes of death

Diffuse peritonitis	4	
Multiple abscesses	2	
Paralytic ileus	1	
Pulmonary embolus	4	
Lung abscess and pneumonia	1	
Addison's Disease	1	13

### Clinical findings

Simple acute appendicitis	1
Acute with perforation or gangrene	9
With localized abscess	2
With localized peritonitis	2
With diffuse peritonitis	5

Autopsies 6, or 47 per cent

## HENRY FORD HOSPITAL APPENDECTOMY FOR ACUTE APPENDICITIS DURING LAST TEN YEARS

Deaths	Years	Cases	Mortality
13	10	1405	0.92%
7	9	1234	0.57%
6	8	1069	0.56%
3	7	891	0.34%
3	6	709	0.42%
1	5	601	0.17%
0	4	466	0.00%
0	3	325	0.00%
0	2	190	0.00%
0	1	108	0.00%

DR JOHN S. LOCKWOOD, New York. It is a pleasure to have the opportunity of discussing Dr. Schullinger's paper and to remark first on the fact that Dr. Schullinger has acted as a very efficient one-man committee in Presbyterian Hospital for a number of years in carefully following our experience with acute appendicitis and keeping close tab on the results. In spite of the splendid record many hospitals can now present, I do not think we ought to become in any way smug about the results, because patients with peritonitis still show a significant mortality rate. In analysis of the explanation for the progress in the last few years, I think the outstanding accomplishment has been through recognition of the fact that peritonitis is a local disease which produces a very profound systemic reaction and that in effect, it causes death through shock, and the methods of treatment of peritonitis which have been conspicuously effective have been those which increase the patient's tolerance to the shock-promoting factors in the disease, more delib-

erate, careful pre-operative preparation, correction of metabolic, electrolyte and water balance, use of blood, plasma and oxygen, gastro-intestinal decompression and, finally, administration of chemotherapeutic and antibiotic agents. Obviously, it becomes exceedingly difficult to evaluate in any mathematical way the relative significance of any one factor in treatment, and certainly that is true so far as chemotherapeutic agents and antibiotics are concerned.

Through the opportunity I have had during the last three years to study the physiologic aspects of experimental appendicitis in the dog, I have become convinced that an important role of chemotherapeutic and antibiotic agents is their ability to modify the severity of the toxic reaction of the host to bacteria and bacterial products in the peritoneum. One effect of the sulfonamides, penicillin and streptomycin is to interrupt bacterial synergism, which is of outstanding significance in this type of peritonitis. Even though the drugs may not be active against all the flora involved, their ability to restrain growth activity of gram positive cocci seems to modify the tendency of the disease to spread. Second, there is the ability of the sulfonamides and penicillin to limit the production of bacterial toxins and thereby to minimize the "dose" of toxic protein split-products which the patient must absorb. One mechanism we have been interested in is the apparent ability of the sulfonamides and penicillin directly to neutralize the action of the toxic bacterial proteins which are elaborated by the types of organisms involved in peritonitis. And, finally, of considerable importance is the ability of these agents to encourage production of a fibrin barrier around the focus of infection.

DR GROVER C PENBERTHY, Detroit. At the meeting of this Association in 1942, Drs Benson, Weller and I reported a study of 1653 cases of appendicitis covering a 15-year period (1927-1941) at the Children's Hospital of Michigan. The mortality in the acute ruptured diffuse peritonitis was 64.9 per cent, with many of this group moribund on admission. The over-all mortality, including all types, was 4.2 per cent.

In the period 1939-1941 a study of the group with peritonitis or abscess was made, as to the effect of chemotherapy on the mortality rate, and in the 47 cases treated with chemotherapy the mortality was 2.1 per cent, in the 67 cases not treated with the sulfa drugs the mortality was 11.9 per cent.

In contrast with the above, from 1942 through 1946, 435 infants and children have been operated upon for appendicitis, of this group 104 had perforated appendices with peritonitis. These patients have had the benefit of surgery and chemotherapy, which represents both sulfa and penicillin therapy, in addition to adequate amounts of blood combined with fluids sufficient to maintain a proper mineral and electrolyte balance with control of distention by intubation and suction drainage. In this entire group of 435 patients there has been no mortality. Fewer of the patients with peritonitis have had peritoneal drainage and it is our belief that it has reduced the incidence of post-operative intestinal obstruction.

Our study confirms the results reported by Dr Schullinger, and we congratulate him and his associates on their results.

DR JOHN A MCCREERY, New York. It might be of interest to compare Dr Schullinger's results with those of a suburban hospital of 150 beds in which most of the surgery is done by seven or eight men who probably have not the same average ability or experience as the visiting staff at the Presbyterian. This may be balanced by the fact that the community is intelligent and health conscious, as evidenced by the fact that more than 70 per cent of our cases have been operated on within 24 hours of the onset of symptoms.

In 1941 Dr Serrell and I published in *Surgery*\* our results in 525 cases of acute appendicitis operated on in the Greenwich Hospital during the period from June 1, 1933, to December 31, 1939. In this series there were seven deaths, one in a patient with local peritonitis, the other six with diffuse peritonitis. All these cases died of continuing peri-

\* *Surgery* Vol. 9, pp 349-357, March, 1941.

toneal sepsis During the period from January 1, 1940, to December 31, 1946, there were 515 cases with six deaths In only one of these was death the result of continuing peritoneal sepsis The only change in our procedure in this time is more meticulous care in maintaining fluid balance and the more general use of the sulfa drugs, both local and general, 186 of the 515 having been treated with sulfa Of the six deaths, one was in a patient who was admitted with an abscess, one died suddenly of massive pulmonary embolism while up and about and ready for discharge, one patient had been a hemiplegic for five years and died of cardiac failure The remaining three cases were in the older age group, one 77 and another 70 These three complained of acute abdominal pain from eight to ten days after operation and rapidly developed signs of peritoneal irritation and obstruction At operation all three had necrosis of the terminal ileum thought to be due to mesenteric thrombosis All three had evidence of marked cardiovascular disease

We all hope for a mortality of zero in acute appendicitis, but we must realize that with increasing longevity and the increasing number of patients above 60 years of age, appendicitis may be cured and yet the patient dies of some underlying condition while still in the hospital These cases must be recorded as deaths from appendicitis, which is inaccurate unless statistics are broken down more completely

DR RUDOLPH N SCHULLINGER, New York (closing) The speaker desires to thank Dr Bothe, Dr McClure, Dr Lockwood, Dr Penberthy, and Dr McCreery for their interesting and informative comments Dr McClure's record is one toward which all of us are attempting to strive Dr Lockwood dilated on the protective mechanism in peritonitis, which of course arouses the attention of us all Dr Penberthy's report on the mortality in children is interesting, particularly in view of Dr Taylor's study at the Babies' Hospital in Columbia Medical Center In the period from 1935 to 1939 he found two deaths, and from 1940 to 1944, two deaths So he was not certain what role some of the newer methods of treatment might play in reducing the mortality amongst children Dr Bothe's comments shed additional light on some of the responsible factors in appendicitis mortality between the time of onset of the acute attack and the time of operation Delay and catharsis are not always the patient's fault Dr McCreery's figures are illustrative of the good work accomplished by smaller staffs in smaller institutions, and one sincerely hopes this is true for all other similar hospitals throughout the country

# STUDIES UPON SPINAL CORD INJURIES\*

## I The Development of Automatic Micturition

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MANY OF THE COMPLICATIONS which arise from injury to the spinal cord, other than the paraplegic state, have an important bearing upon the prognosis of the patient. The function of the urinary bladder, the occurrence of root, visceral, and diffuse burning pains, the development of mass reflexes and spasms, dysfunction of the autonomic nervous system, the treatment of decubitus ulcers, urinary tract calculi, and the many psychological and emotional problems which beset the patient are some of the factors which seriously affect his rehabilitation. The care of the patient with a spinal cord injury is not solely one of attempting to make him walk. He presents a serious general medical problem and requires the combined efforts of those well-trained in every field of medicine and surgery. Fortunately, some of these patients improve so that these efforts need not be specifically concentrated but the majority require continued, careful supervision to insure their maximum rehabilitation.

Our studies are based on an experience with 471 patients with injuries of the spinal cord. Of these, 416 were patients injured in military service and 55 were civilian patients. Of the military patients, 115 were examined and studied in an overseas theater of war as early as one hour to two or three weeks after injury and as late as 122 days after injury. Satisfactory follow-up data has been maintained upon 18 of these patients. The other 301 patients were observed in a Veterans Administration Hospital and their histories in some instances cover a period of five years following injury. The civilian patients have been observed in certain instances for as long as 20 years. Among the patients of a military status, 295 received open wounds of the spinal cord from bullets or shell fragments, while 121 suffered closed injuries, exemplified by the common fracture-dislocation of the spine. Among the civilian patients, only eight were injured by open wounds, and 47 sustained closed injuries of the spinal cord. In the two groups of patients with the closed type of injury, traffic, diving, and wrestling accidents were most common.

The establishment of efficient urinary function is one of the primary goals in the care of the patient with an injury of the spinal cord. It avails little to rehabilitate the patient successfully in various other spheres if eventually he does not have adequate control of his urine, for in such a chronically disabled patient the inability to void with some means of control will alone prevent his return to a socially acceptable state. Furthermore, proper urinary function, in so far as it can be developed, is important for the preservation of life itself.

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\* Read before the American Surgical Association, March 25, 1947, Hot Springs, Va

THE IMPORTANCE OF EARLY CARE

Urinary function in our patients has appeared in one of the following five forms (1) early return to normal micturition, (2) eventual return of partial voluntary control of micturition, (3) involuntary dribbling of urine, or the frequent uncontrolled passage of very small amounts of urine, (4) absolute retention, a less common situation, and (5) automatic or reflex micturition, entirely free of any voluntary effort of the patient. If complete, normal urinary control, or partial voluntary control aided by special efforts on the part of the patient to empty his bladder, can not be obtained, the ideal condition is that of automatic micturition. Proper care of the bladder in the early stages of treatment is most important to insure the development of reflex emptying of the bladder when any return of normal power is impossible. Under ideal conditions an indwelling urethral catheter placed immediately after injury, properly serviced, and connected with a tidal drainage apparatus adjusted for the particular needs of the patient, will lead to automatic micturition within a few weeks. The shortest period for such reflex function to become established in our patients was at the end of five weeks, in a patient with a lesion at the fourth thoracic cord segment. Such function was established in one patient with a complete lesion of the conus medullaris and cauda equina at the end of two and one-half months. In both instances the patient had no other type of bladder drainage than that of a small caliber Foley catheter. Tidal drainage was used from the beginning, urinary sepsis was kept at a minimum, urinary calculi did not develop, and the nutritional state of the patients remained good. In numerous instances we have found proof of the efficacy of the indwelling catheter with tidal drainage not only in the establishment of automatic micturition but also as an aid in restoring partial voluntary control. In no case did automatic micturition develop while a suprapubic catheter was in place. On the contrary, many patients developed such urinary control following the removal of the suprapubic tube, placement of an indwelling catheter and training for a period of time thereafter with tidal, or carefully controlled manual drainage. Severe urinary infection soon after injury was found to prolong greatly or obviate completely the development of automatic micturition, and such an infection many times has been observed to destroy an already well established automaticity.

Among the patients of military status, various methods of urinary drainage had been used in the early days and weeks of treatment. These included (1) allowing the bladder to distend and overflow, (2) manual expression, (3) perineal urethrostomy, (4) suprapubic cystostomy, (5) repeated urethral catheterization, and (6) an indwelling urethral catheter. The exigencies of war alter treatment, but it is a moot question as to whether suprapubic drainage is necessary for purposes of transportation. Ample evidence is at hand that many suprapubic tubes, ostensibly placed for such purposes, were initially placed too high or too low and thereafter neglected so that they became the source not only of severe urinary sepsis but also of the additional complication of bedsores. Petroff<sup>1</sup> and other recent writers have pointed out the fact that



the elimination of the suprapubic tube, repugnant to most patients, is an important factor in the improvement of the patient's morale. When a comparison is made between the advantages of early indwelling catheter drainage and prolonged suprapubic drainage, it is immediately obvious that automatic micturition is encouraged by the use of the indwelling catheter and made impossible by the suprapubic tube.

#### THE LEVEL OF THE LESION

Automatic micturition may occur in the presence of a complete lesion at any level in the cord or cauda equina. In 77 patients with cervical lesions, 11, or 14.3 per cent, eventually developed automatic micturition. In 288 patients with lesions at various levels of the thoracic cord, 97, or 34 per cent, eventually developed such reflex activity. In the 106 patients with lumbo-sacral lesions, 17, or 16.4 per cent, developed automaticity. Under favorable conditions, therefore, automatic micturition may develop and continue regardless of the level of the lesion. It is not uncommon for the automaticity to be interrupted and require a secondary period of training when such complications as urinary sepsis, calculi formation, nutritional debility, decubiti, or severe mass reflexes occur. Automatic micturition develops most rapidly when the lesion lies below the 7th cervical cord segment and above the 5th thoracic. There is an increase of the time required for its development as the incidence of the lesions descend into the lower thoracic cord, and most patients with lesions of the conus medullaris or of the cauda equina require from 8 to 20 months, or longer, to develop automaticity. Therefore, our experiences corroborate the fact pointed out many years ago by Head and Riddoch<sup>2</sup> that the completely isolated bladder without any intact distal segment of spinal cord can under the proper conditions develop and maintain the state of automatic reflex emptying.

Severe retention, as well as frequent dribbling of urine, with large residual capacities up to 1,200 cc. in either condition, has been observed in the presence of a complete or partial lesion, at any level of the cord or cauda. We have found numerous instances of dribbling with high grade retention in many of our patients with cervical or thoracic cord lesions whose early care was punctuated with many complications, or who were early denied the benefits of an indwelling urethral catheter and tidal drainage training. The occurrence of severe mass spasms of the extremities is of common occurrence with lesions of the cord, and severe spasms usually so affect the bladder that it takes part in the general somatic spasm and tends to evacuate small amounts of urine at frequent intervals. Under such conditions it may contract down to a very small capacity, usually with little or no residual. These mass spasms affecting the bladder and lower extremities are of decreasing incidence as the lesions descend the cord and cauda below the 10th thoracic segment.

In the presence of lower thoracic or caudal lesions, where there is still some power of contraction in the abdominal muscles, the patient is aware of the need to void by such signs as a feeling of abdominal distention, burning or

tenseness in the genitalia, suprapubic cramping sensations, or tenseness, burning, and drawing sensations in the lower extremities. When the lesion lies above the 9th or 10th thoracic segments, distention of the bladder and a warning of impending micturition may be manifested by such signs as flushing of the face, arms and chest, perspiring on the upper half of the body, a feeling of sudden heat over the face and neck, nausea, or sudden severe headache. In the rare patient these latter signs may also be present with lower thoracic or caudal lesions, but in any event the symptoms are promptly relieved upon the emptying of the bladder. Upon becoming aware of such signs, many patients can initiate urination by such extravesical stimuli as massaging the lower abdominal wall, rubbing the skin of the inguinal region, tugging on one spermatic cord, or pinching the skin of the thigh. Patients with lesions of the conus or cauda do not respond as readily to such extravesical stimuli as do those with higher lying lesions. Yet if they are unobstructed at the bladder neck they may eventually develop some particular stimulus which will aid starting of the urinary stream, and while their automaticity is less likely to be efficient, they can aid the emptying of the bladder by suprapubic pressure and by holding the breath and tensing the abdominal muscles.

In those patients who void every 2 to 15 minutes in small amounts and who usually hold a large residue of urine, the least straining such as coughing, sneezing, laughing, or hearing a sudden loud noise may cause them suddenly to wet themselves. Such patients are therefore forced to keep in place a urinal, to wear a clamped off urethral catheter, to use a penis clamp, or to wear a rubber urinal, none of which is an ideal situation for the control of the urine. Many of these patients are found to have greatly hypertrophied bladder necks, and the operation of transurethral resection of the ring of hypertrophied muscle has been successful in transforming such patients into a state of automatic micturition, with almost complete emptying every one to three hours. They are frequently relieved, also, of the uncomfortable burning in the groin, flushing of the face, perspiration and headache which accompany such frequent spasmodic attempts of a bladder working against resistance. Not only is the patient freed of a restraining and embarrassing condition, but the bladder, without a high residual urine, shows a much cleaner urine following such an operation.

The amount of residual urine in the automatic bladder varied widely among our 471 patients. Of these patients 26.3 per cent, or 125, eventually developed automaticity, or had it over a period of time during some phase of their observation. Residuals have been found varying from a few cubic centimeters to as high as 500 cc. It can not be said that a bladder which acts reflexly every two or three hours but which leaves behind a high residual content is a successfully functioning bladder, and residuals as low as 50 cc or less may lead to sepsis or calculus formation. It has been common to find patients who were discharged to their homes for a period of time, with good automatic bladder function, return to the hospital weeks or months later with nutritional difficulties, decubiti, or urinary sepsis, with complete or nearly

complete loss of their automatic micturition. We have been impressed by the ease with which automatic activity of the isolated bladder is altered or lost. Such reflex activity needs constant aid and supervision, but even once lost it can be re-established by patient care through the use of an indwelling catheter, tidal drainage or carefully managed manual irrigation, and the elimination of such complications as have been named.

#### THE EXTENT OF THE LESION

It is not always possible to determine accurately the degree of residual neurologic function in the incomplete lesion of either the cord or the cauda equina, and likewise the degree of voluntary control over urination can not always be determined. Any patient who can actually feel the passage of urine within the urethra obviously is not voiding by automatic micturition, though it is true that in such patients the act may be started by an extravesical stimulus such as massage of the groin. Partial voluntary control and the effectiveness of extravesical stimuli may exist simultaneously. Urinary sepsis, calculus formation, and a large amount of residual urine may exist in these patients as they do in those with complete neurologic lesions.

One patient was seen who sustained a stab wound of the spinal cord at the midthoracic level, with a resulting most accurate Brown-Sequard syndrome. At no time did he ever have any loss of voluntary control over urination. Four other patients who sustained shell fragment wounds of the lower cervical and upper thoracic cords with a production of modified Brown-Sequard syndromes were seen early after injury, and they likewise did not suffer any urinary difficulties.

#### SUMMARY

Automatic micturition will develop following a complete lesion at any level within the spinal cord or cauda equina. It appears earlier and with greater efficiency in the presence of lesions between the levels C 7 and Th 5. It does not appear in the presence of incomplete lesions of the cord, though the effect of extravesical stimuli on the initiation of urination may be quite similar in the case of either a complete or partial lesion. Extravesical stimuli are in any event less effective in the presence of lesions below the 10th thoracic segment. Automatic micturition may occur with remarkable regularity at intervals as long as three hours, but with very low efficiency as determined by a large residual amount of urine. Lesions of the conus and cauda do not produce the striking viscerovisceral reflexes, such as flushing, perspiring, headache, or reverse peristalsis such as may appear in the presence of high lesions in the cord, and the appearance of such reflex phenomena in severe form, with or without massive spasm of the lower extremities, may spell the termination of efficient automatic micturition.

Cystometric examination at regular intervals will indicate when the catheter may be removed to allow the trial of automatic micturition, indicating that a reflex response to bladder wall tension is necessary for this activity.

Automatic micturition will develop only when there is no mechanical bladder neck obstruction and when the sphincter is capable of reflex relaxation. Extravesical stimuli are an aid but not a necessity to the development and maintenance of automatic micturition. Automaticity will not develop in the patient with severe bladder sepsis, multiple calculi, or a condition of severe debilitation.

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# THE CONTROL OF CANCER\*

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## INTRODUCTION

THE DEATH TOLL FROM CANCER has been steadily rising, chiefly due to the older average age of the population, and last year there were 181,000 dead. Since cancer is not a reportable disease, there are no accurate figures on incidence, but surveys<sup>1</sup> indicate there are approximately 310,000 new cancer cases each year. It is estimated that there are 700,000<sup>2</sup> persons in this country who are under treatment for cancer at any one time. There is evidence of increasing public interest in the control of cancer as shown by a recent Gallup survey, which indicated that 72 per cent of the people were willing to pay more taxes in order to have better control of cancer.

The control of cancer requires research, education, and service to the cancer patient. All this involves the medical profession, the hospitals, the public health service, nursing service, schools, universities, and other groups. Obviously, no one agency, governmental or private, has sufficient resources to cope with a problem of this magnitude. The necessity for seeking the assistance of all groups is apparent. The keynote of effective cancer control must be the cooperation and coordination of all groups dedicated to this task. Since the voluntary health agency exists for the purpose of assisting the people to meet a health menace not controlled by other organizations, its most important function may be as a coordinating agency.

The American Cancer Society may best serve the people and the medical profession by remaining a dynamic force, so flexible that it may render assistance wherever the need is greatest, rather than to become static by assuming a permanent maintenance responsibility. Its most valued service may be to show the need, point the way to better cancer control, and demonstrate the method by which this may be achieved. The ultimate goal of the voluntary health agency is to bring disease under control, and so to eliminate itself by removing the reason for its existence.

## OVERALL PLANNING

The need for a more intensive effort to control cancer is apparent. The scope of the various activities involved in the control of cancer is so great that no one group, the medical profession, the U S Public Health Service, the American Cancer Society, or the private foundations can accomplish the goal unaided. For this reason there is a need for a cooperative, coordinated effort within the framework of an overall plan of attack. This is necessary if the most effective use is to be made of our limited resources, men, and material.

Funds available for the support of cancer research in the past have been

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## CONTROL OF CANCER

inadequate, but even if adequate financial support were available, overall planning is needed in the interest of economy and efficiency. During the year 1946 the funds available for cancer research were as follows:

American Cancer Society	\$2,500,000
U. S. Public Health Service	1,772,000
All private foundation funds	650,000
Total	<hr/> \$4,922,000

Thus our national expenditure for cancer research was at the low rate of \$27.19 per death caused by cancer. At the same time we live in an economy where more than this amount was spent to advertise one brand of cigarettes and four times this amount was spent for hair tonic. Plainly, as a nation we have not given due consideration to the facts and the resources needed for an overall attack to control a major health menace.

There is also a shortage of trained personnel and facilities for both research and the care of the cancer patient. Since time will be required to build laboratories and hospitals and even more time to train personnel, the need for a coordinated overall plan rather than competition between interested groups is apparent.

The control of cancer may be accomplished by two major lines of attack:

1. The maximum use of the present methods of prevention, diagnosis, and treatment.

2. Research for new methods.

The only methods at present available for the treatment of cancer are surgery, x-ray, and radium. The importance of surgery in the treatment of cancer, the importance of cancer to the surgeon, and the public interest in this problem warrant a discussion of the role of surgery.

In order to make the maximum use of surgery in the prevention, diagnosis, and treatment of cancer there are four objectives to be achieved:

1. Early recognition of the signs and symptoms of cancer is necessary so as to cause the potential patient to seek the advice of a physician early in the course of the disease. While this is a problem of lay health education, the content of knowledge is medical. Further, while this problem more properly lies within the field of activity of the lay educator, the general practitioner, and the internist, the surgeon because of his wider experience in the treatment of cancer has a responsibility in promoting such education. Unfortunately, all cancers do not give early signs and symptoms, or they exist in a part of the body where they cannot be seen or felt by the patient. For some time, regular semiannual physical examinations have been advocated to meet this problem. Cancer detection centers or prevention clinics have been set up in New York, Philadelphia, Chicago, and other cities. These clinics have reported finding approximately 15 per cent of cancer in supposedly well persons. This is more cancer than has been estimated to exist in our population. Statistics as to the incidence of cancer, however, are so inadequate that these figures may be more nearly correct than the previous estimates. Macfarlane<sup>3</sup> found 10 can-

cers in 10,325 examinations in 550 female volunteers, an incidence of 2 per cent or 0.1 per cent of the examinations. In addition, numerous other abnormalities requiring medical attention were detected. *There is no doubt that regular physical examinations will detect many unsuspected cancers in an early curable stage of the disease.* It appears that the value of the semiannual physical examination should be measured in terms of the general health problem and its educational value, rather than in terms of cancer alone. If a semiannual physical examination is to become part of our national health program, a re-evaluation of the number of physicians required for the nation is indicated. Approximately 95 per cent of all cancers are found in the 59,000,000<sup>2</sup> people who are over 35 years of age. Assuming one-half hour per examination, a biannual physical checkup would require 59,000,000 physician hours, or the full time of approximately 30,000 physicians. It should not be assumed that this is an impossible task because of the number of physicians required, nor that cancer detection or health maintenance centers could be put into operation immediately for the entire nation. Rather it emphasizes the need for planning, because if such a national program is to be realized within a ten-year period, we must plan now to train the necessary personnel and provide the required facilities. In the meantime, the need for cancer detection\* in supposedly well persons is established, and every effort should be made to extend its application. There is need for data to determine the type of history and physical and laboratory examination which may yield the maximum result with the greatest economy.

There is an urgent need for medical schools and hospitals to establish pilot cancer detection or health maintenance centers to study these problems and to establish techniques for screening large groups of the population. Such pilot clinics may also provide an invaluable service as postgraduate teaching centers. Medicine as a social science must face this problem, the scope and importance of which demands an experimental approach to insure acquisition of basic information.

Surgery cannot yield a high degree of success unless cancer is treated before the disease has spread to distant parts. It is, therefore, apparent that the public must know what potential cancer symptoms are so that it may seek aid early in the course of the disease. It is also well established that many cancers do not give early symptoms but can be detected on physical examination. While the relative value of lay health education and the regular physical examination has not been determined, it is apparent that both are necessary steps in effective cancer control. Finally, for those cancers which do not give early symptoms and which cannot be detected on physical examination, research is needed to establish more effective screening technics.

2 The second important objective is early diagnosis, which is primarily a responsibility of the medical profession. The physician is directly liable for

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\* The term detection is here used to indicate the detection of cancer in supposedly well people who have no complaints. It is suggested that the word prevention should be limited to the eradication of supposedly precancerous lesions.

the delay in 25 per cent of cases and shares the responsibility with the patient in another 15 per cent <sup>4, 5, 6</sup> While the patient is culpable for most of the delay in superficial cancer, the physician assumes the major responsibility as the cancer becomes more inaccessible, requiring special laboratory, x-ray, or endoscopic examination. This points the need for better professional education in the diagnosis of cancer, since wrong advice is frequently given. It also suggests that lack of availability of proper diagnostic facilities may be an important factor. There is too frequently a tendency to treat cancer of the internal organs as a benign or functional lesion until proven to be otherwise. This does not imply a knife diagnosis, but earlier and more adequate study if the cause of the complaint is unknown.

It behooves those of us who are teachers of medicine and surgery to inquire as to why this situation should exist. Are our textbooks so written as to make clear that cancer of the internal organs, such as the lungs and gastro-intestinal tract, cannot be diagnosed by the history and physical examination? Do we spend too much time demonstrating advanced cancer and too little emphasis on the steps necessary to diagnose early cancer? Is the training of specialists on a sufficiently broad basis to make clear the danger of inadequate general physical examinations? Does the instruction in physical examination make clear its limitations as well as its potentialities?

As lay health education becomes more effective, causing an alert public to seek earlier diagnosis, the diagnostic problem for the physician will become more difficult. Has the time come to re-evaluate some of the criteria we have used in teaching the diagnosis of cancer in the past? In an already overcrowded curriculum, is adequate time and skill devoted to the second most common cause of death?

It is clear that the average physician is increasingly in need of help in the diagnosis of early cancer. More studies are needed to indicate what type of assistance, in what age groups, and where it is most needed. Are facilities for diagnosis available to the average physician adequate to meet the need? Have we devoted sufficient attention to postgraduate education for the doctor who is not privileged to work in a hospital or medical school? The American Cancer Society, believing that there is a need for postgraduate cancer education, proposes to publish a concise professional journal dedicated to this purpose. Until such time as research makes available better and simpler methods of diagnosis, we have no choice but to make the maximum use of the methods we now have.

3 The third requirement is prompt treatment. Early detection and diagnosis may be of little value unless treatment is rendered promptly. Procrastination by either the doctor or the patient may be fatal. The "shopping" habit of patients going from one doctor to another seeking a favorable opinion and general lack of health education contributes to delay. Also in recent years the shortage of hospital beds, with delays in admission because of long waiting lists, is a contributing factor.

4 The fourth objective is adequate treatment. Until research reveals new



and better methods of treatment, the chief hope of the cancer patient lies in surgery. The developments in surgery have been great and show promise of keeping pace with the increased demands of cancer patients if treated in time. There is, however, a lag between the potentialities of treatment as demonstrated in the best clinics and the average result found in the average hospital available to the average patient. This is of especial significance, because the average physician is more likely to be influenced by the results he has experienced in his own patients rather than those reported in some far away clinic. There is a great need to study the results of treatment in larger and unselected groups of the population, and to find ways and means of making better treatment available to more people.

The Tumor Committee of the Connecticut State Medical Society in collaboration with the State Department of Health in 1934 developed a system for the study of cancer in 27 general hospitals. This offered the first opportunity to determine the effectiveness of present methods in treating cancer in a large section of the population. The first study was done on 1,610 cancers of the rectum admitted to hospitals between 1935-45.<sup>7</sup> During 1935-40 the radical operability was 32 per cent, and during the second five-year period it rose to 44 per cent. For the same period the largest clinic in New England reported an operability of 83.5 per cent.<sup>8</sup> During the first five-year period, the operative mortality in the 27 general hospitals was 25 per cent, and during the second five-year period it dropped to 18 per cent. At the same time the operative mortality for the largest clinic in New England was under 5 per cent. The five-year cure rate for the 735 patients in Connecticut was 7.9 per cent in contrast to approximately 50 per cent for those patients entering the larger clinics.

These comparisons are not made to show that one clinic is better or worse than another, or selective, but to call attention to the fact that the average effectiveness of our present methods of treating cancer in a large group of the population is vastly different from those ordinarily reported in medical literature. The larger clinics have pointed the way and demonstrated what may be accomplished. It is the responsibility of those interested in cancer as a health menace to obtain the facts and point the way to better treatment.

The statement has been made that 30-50 per cent of those now dying of cancer could be saved by the maximum use of the present methods. It is estimated that there are 14,000 new cancers of the rectum in this country each year. If we assume the present five-year cure rate is 10 per cent, there would be 1,400 cured patients each year, leaving 12,600 who die within five years. To save 50 per cent, would require a curability approximately 5 per cent under the cure rate reported by one of the larger clinics today. It would therefore, appear that an attempt to save 50 per cent of those now dying from cancer of the rectum is not an unreasonable goal.

#### CANCER RESEARCH

The second major line of attack on the cancer problem is research for

new and better methods of prevention, diagnosis, and treatment. While there is no longer a question of the need for cancer research, there are, however, differences of opinion as to how funds may be most wisely expended, and what methods and disciplines are most urgently needed. This appears to be a natural consequence of the rudimentary state of our knowledge of cancer and diversity of interest in the problem. There is, however, a consensus of the need for more fundamental knowledge of normal growth so as to better understand the abnormal growth of cancer.

The present high development of surgery well exemplifies the wisdom of the flank attack versus the frontal assault. Discoveries in supposedly unrelated fields have made modern surgery possible. From Pasteur and wine fermentation to bacteriology and asepsis, the chemistry of ether and laughing gas to anesthesia, the chemistry of aniline dyes to chemotherapy, the physiology of moulds to penicillin, these are all examples of the potential benefits of the prepared mind on a broad research front. At the same time, the rapid development under wartime pressure of penicillin and blood substitutes are effective examples of the frontal assault by planned developmental techniques.

#### THE SCOPE OF CANCER RESEARCH

The complexities of the problems and the varied disciplines required all suggest the need for coordinated and integrated effort. For these reasons the American Cancer Society turned to the National Research Council's Committee on Growth for advice and guidance in planning its research program. The Committee on Growth is composed of 19 members with an executive committee, the members of which are chairmen of the divisions of physics, chemistry, biology, clinical investigation, chemotherapy, and fellowships. Each division is composed of a number of panels made up of specialists in their respective field of research. The Committee on Growth, together with the panels, numbers 120 scientists representing 48 different universities and laboratories. Requests for grants-in-aid are received by the secretary of the Committee on Growth at the National Academy of Sciences in Washington, D. C., where they are channeled through the various divisions and referred to the panels best qualified to advise on the research for which funds are requested.

Thus requests for grants-in-aid receive careful study by experts in each panel, and the chairman of each division presents his recommendations to the executive committee for final consideration, so that funds may be allocated according to the overall need. It is hoped this plan will insure that the most promising research receives adequate support, that duplication of effort may be avoided, and that eventually a better coordinated and integrated attack on cancer may be developed.

It is recognized that grants-in-aid may not provide sufficient latitude for the development of cancer research. It is expected that grants may be initiated to stimulate research in responsible institutions with established reputations

and that such funds may be used within a limited but less restricted field than the grants-in-aid

Finally, as the need arises, it may be necessary to provide funds for developmental research, using more intensive or compartmentalized methods within institutions especially equipped and staffed for this purpose

There is a shortage of personnel trained in the disciplines needed in cancer research. In order to fulfill this need the American Cancer Society has made funds available for research fellowships up to a maximum of \$6,000 per year for senior fellowships. Beyond this, it is hoped that more permanent posts will become available in the various universities and laboratories. It appears that one of the reasons for the scarcity of qualified personnel may be that in the past cancer research has been so frequently a dead-end street academically. It is essential that opportunity be provided for adequate careers in this difficult field of investigation.

There has been much discussion as to the place of cancer research in medical schools and whether departments of oncology are justified. It is frequently observed that no one individual can be competent in the whole field of cancer. The same reasoning could be applied equally well to a professor of medicine or surgery and in fact, this is acknowledged by the subdivision of these departments. It appears that a serious approach to the study of cancer cannot long remain an avocation, and it is likely that tradition will make a place for new ideas within the old framework.

The study of cancer began at the bedside of the patient. It moved to the mortuary and the laboratory, but finally it must return to the patient. Clinicians are the custodians of the care of patients, and hence have a grave responsibility in cancer research. Theirs is the task of promoting research in this difficult field at the bedside. The study of cancer in the clinic has yielded the only effective modes of therapy yet available, and among these is surgery. The surgeon must now assume his obligation by participating in the teamwork needed to bring together the varied disciplines required in the new and highly specialized technics of clinical investigation.

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DISCUSSION—DR E P LEHMAN, Charlottesville, Va You have heard presented in very brief form the program of the American Cancer Society The surgeon comes closer to the cancer patient, if only because of the need for biopsy, than does any other group in medicine For that reason the American Cancer Society, and especially its Medical and Scientific Committee, recognizes the importance of having its program presented to and understood by this most representative group of surgeons of the country I know and Dr Oughterson knows that there are members of this Association who have in the past expressed disagreement with the aims and policies of the American Cancer Society There may be good reasons for such disagreement The Society in growing in two years from a corporation spending \$800,000 a year to one spending \$10,000,000 a year has made mistakes It needs the wholehearted support of the surgical profession The Medical and Scientific Committee will, therefore, welcome constructive criticism from any member of this body transmitted through Dr Oughterson Cancer is the leading problem of the surgeon today The American Cancer Society is in a sense your instrument in a program of cancer control in which we are all so vitally interested

DR A W OUGHTERSON, New York (closing) I can only second what Dr Lehman has said Ours is a common effort against a common enemy, devoted to the common purpose of trying to find a common solution It is our earnest desire to promote the control of cancer in the best interests of the medical profession and the nation, and we welcome your assistance and advice at all times

# THE SPECIALTY OF ANESTHESIA \*

and its Application

in the Harvard University-Massachusetts General Hospital Department

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## I THE SPECIALTY OF ANESTHESIA

FACTORS THAT INFLUENCE the specialties of medicine in large part shape medical practice. It is desirable, therefore, to consider the factors of current importance in the development of anesthesia. In this, emphasis will be placed on the problems of the university and the university hospital. The anesthetist can occupy a fortunate position in these and in other institutions, if he will take advantage of his opportunity. I should like to be specific, that is, to set down what this opportunity seems to be at the present time, in terms of the strength and the weakness of anesthesia as a specialty, and then to describe, as a working example, how the views presented here have been put into practice in the organization and development of our Department.

In the first place, one must admit that a stigma is attached to anesthesia. To deny this is to evade the facts. It does exist, it need not. The plain fact is a stigma will continue to be present until anesthesia can attract its share of able men, men who are as able as those who go into other fields of medicine. Great progress has been made by those who have been leaders in anesthesia over the past 20 or 30 years. Their good work needs to be built on and carried forward. Clearly the central problem of anesthesia as a specialty is how to attract good men. Some aspects of this will be discussed. Grim denial that the field has weaknesses has not hidden them. It is better to face them, but at the same time some of the strong points of the specialty can be considered.

### SOME WEAKNESSES

*Technics Alone Are Not Enough.* Anesthesia is not rich in technics, nowhere nearly as rich as surgery is. This in no way minimizes the importance of the essential anesthesia technics, but to try to attract good men on this basis alone is to fail. To insist that as much time is necessary for the technical training of the anesthetist as of the surgeon is to take an indefensible position. And yet such stands are common.

Although experience over considerable time and range of material is required for expertness, anesthesia technics can be mastered by ordinary men who are ordinarily deft, with only a modest requirement of intelligence and of knowledge and of judgment. As clinical anesthesia is taught today there is an almost overwhelming preoccupation with tools and their use. Current teaching too often stimulates only a pursuit of technical skill.

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\* Read before the American Surgical Association, March 25, 1947, Hot Springs, Va.

Anesthesia was developed in the clinic and has been nourished chiefly by clinicians. This may be part of the trouble. In recent years medical specialties have, to a great extent, grown through laboratory advances. Anesthesia has not fared as well on its clinical nourishment as other specialties have on a richer diet. Men who are occupied entirely in the clinic have neither the time, nor in many cases the training, to furnish their specialty with the vitality it needs for growth.

*The Laboratory vs Clinical Empiricism* In anesthesia we see an example of what happens when medicine attempts to advance chiefly through the clinic, inadequately concerned with basic problems. It is inefficient, it advances by trial and error. The weakness of this is measured in terms of lives needlessly lost. But the discouraging fact is that anesthesia must continue to depend greatly upon empiricism, at least for the time being. The almost complete mystery surrounding the mechanism of the anesthesia process itself and the invulnerability of the mystery to such attacks as have been made upon it, have done much to discourage investigation in this complex field.

Perhaps more than any other factor, the development of anesthesia has been delayed by our ignorance of the anesthesia process. One can liken the position of the anesthetist when confronted by the anesthesia process to that of the internist when confronted by a disease of unknown etiology. Under such circumstances the internist must be guided by symptomatology, and in acting on this basis he may be quite successful. Similarly, the anesthetist's handling of the anesthesia process can be conducted with considerable success on a controlling basis of symptomatology. But just as the internist's treatment of disease usually becomes enormously more efficient once he understands its etiology, so will the handling of anesthesia become much more precise once we understand the mechanism of the anesthesia process.

With the advance of science, even though the mechanism of the anesthesia process remains obscure, rational procedures in anesthesia are possible, yet anesthetists are often so dominated by traditional use of the empirical that they pass by opportunities for rational procedure. They have reached out and taken, for example, agents from the chemist and applied them hit or miss in anesthesia, disregarding the information available from the physiologist and pharmacologist and pathologist concerning these same substances, at the expense of lives. A search through the literature of anesthesia reveals little rational basis for much of it.

There is no need to labor the point that the achievements of modern medicine are greatly indebted to the laboratory. The only thing to remark is that here, at least until recently, an important division of medicine often disregarded it.

*Fundamental Advances Have Rarely Been Made by Anesthetists* Too few of the chief workers in anesthesia have been creative in the sense of making fundamental contributions to the specialty. Anesthetists have developed and polished and increased the efficiency of processes discovered or created by those whose chief interests lie in other fields. Anesthesia has had to depend

upon casual contributions from other workers. These other men have provided the spark, anesthetists have, in the main, only fanned it. And herein, it seems to me, lies one of the most serious shortcomings of the specialty, a shortcoming that must be corrected before anesthesia can mature as a specialty. It is, surely, a great service to introduce advances from other fields into anesthesia. That is not the point. To live a vigorous life a specialty must have not only those who can apply the developments of others but also those who can create new ones. As long as its intellectual life is parasitic, the specialty will never develop satisfactorily.

#### ANESTHETIST AS INVESTIGATOR

The anesthetist may be a third-rate investigator or he may be a good one, but if his abilities and standards are high, he can be an invaluable associate of the professor of pharmacology. The final evaluation of all drugs used in man must be made in the clinic. The pharmacologist needs and ought to use his clinical associate quite as much as the other way around.

Well-established examples indicate that fundamental contributions in physiology are coming from new sources. Basic information is coming out of the clinic and at the hands of clinicians. I venture to say, as examples from my own hospital, that the contributions of Fuller Albright to the physiology of the endocrine glands are important, that Walter Bauer knows more about the physiology of the joints than anyone else. Human physiology turns out to be less comparable to that of the dog or the frog than some have supposed.

A few years ago a distinguished anesthetist, speaking in Boston, emphasized the importance of anesthetists sticking to the clinic and passing up any urges to do fundamental experimental work. These remarks of his were challenging, and coming from such a source, deserve consideration. But they ignore a trend in modern physiology—the shift of emphasis from animal physiology to human physiology, dependence where possible upon observations made in man rather than upon observations in animals. There are a number of problems that the well-trained, soundly grounded anesthetist is in a better position than almost anyone else to investigate, granting that he is not overwhelmed by routine work and that he possess the native ability and energy to do original work of good quality.

The physiologic response of man to drugs must often be tested out in hospitals where “basic” scientists rarely appear. If the trends of medicine show anything, they indicate that the anesthetist who heads a university’s department ought to be capable of profiting by his opportunity to study man. In hardly any field of clinical medicine is such opportunity greater or its utilization more urgently needed than it is in anesthesia. Both basic scientist and clinician can make important contributions to the field of anesthesia. It is the obligation of the man who heads the university’s department to do so.

The technical demands of surgery are so great that the successful surgeon will not often have adequate time to carry on investigation. It is one of the

great advantages of the field of anesthesia that the anesthetist can have such opportunity

#### ANESTHETIST AS TEACHER\*

Why should anesthetists completely relegate the basic instruction in their field to others (pharmacologists)? Is anesthesia so encumbered with difficulties, exacting technics, and demands against time that there is no opportunity for practitioners in this field to encompass the full demands of the specialty? If all responsibility for basic instruction in the field is given up, this will take away much of the intellectual interest and leave the technics. These alone will rarely attract the good man. Such action if embarked upon generally will give a disastrous blow to the specialty. It would be inaccurate to deny that this tendency is present, but isn't its very existence the result of too narrow a view of the field?

Is the university, then, to relinquish in the field of anesthesia all scholarly intent and say, in effect, bring on your technical specialty, admitting that in this division the university will give up its traditional ideals of scholarly workers in all of its parts and accept here a sort of trade-school level as the best it can do?

#### ANESTHETIST AS CLINICAL SPECIALIST

There is a clinical problem of compelling interest in this field. Most able men will not find it in the repeated application of clinical technics, but in applied pharmacology, in the hazards and rewards of translating material from the basic sciences into clinical use. To succeed in this sensibly and safely requires insight and judgment. Clinical anesthesia offers a continuing interest of this kind.

Anesthetists must assume wider burdens than those of clinical anesthesia in its specific sense. The treatment of shock, resuscitation (and this includes aspiration bronchoscopy), certain problems of aviation medicine, gas therapy of various kinds, sedation, these are all reasonable clinical fields for the anesthetist. Anesthetists can be the physiologically-minded guides of therapy in preparation for, during, and immediately following the rigors of surgical intervention. A broad medical background is indispensable for this, as for leadership in other fields. The importance of this essential background is often unwisely minimized by anesthetists.

The act of surgery is a complicated thing, influenced by knowledge and judgment, of course, and by various physical elements—hemostasis, asepsis, anesthesia. Whether anesthesia is or ever shall be a distinct specialty interests me very little. This is by no means a casual dismissal of the importance of anesthesia, it is an affirmation that *clinical* anesthesia is an integral part of

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\* Details concerning teaching are discussed in the following section on the "Harvard University—Massachusetts General Hospital Department of Anesthesia."



surgery, as inseparable from it as hemostasis. If one accepts this view, it seems to me that what validity there is in the claims of anesthesia to being a separate specialty lies in its administrative requirements and in its teaching and developmental aspects, more than in its clinical applications. To relinquish the teaching and developmental, as some do, is to leave little but the technical. If anesthesia is to be a specialty, then it must encompass all of these things. Herein, of course, lies the great vulnerability of anesthesia as a separate discipline. Unless its base is broad enough to include these things, its separateness as a specialty may collapse, for if limited to its clinical activities alone, it will rarely attract the good men who are essential to its development as a specialty. I emphasize again that such a concept does not minimize in the least the importance of anesthesia.

This concept has the not inconsiderable advantage of emphasizing a point too often lost sight of by the anesthetist. That he is a physician engaged in the practice of medicine, not a free agent rattling around in an isolated domain. Too often the anesthetist becomes so preoccupied with the technics and tools of his field that he loses his interest in medicine and whatever knowledge he had of it.

There is a tendency to permit the anesthetist to become established as a "specialist" without the broad apprenticeship of general hospital training in medicine or surgery required of *all* other men who look forward to activity as specialists. It is difficult to see how any man can claim to be a sound specialist in any field of medicine without this essential foundation.

#### ANESTHESIA IS AT ONCE SIMPLE AND COMPLEX

The very ease with which the simplest forms of clinical anesthesia can be administered has until recent years allowed almost the entire specialty in this country to rest in the hands of nurses, or physicians whose equipment is mainly limited to the technical, individuals who could not be expected to make advances. This statement is in no way intended to reflect upon their faithful and in many cases competent services in allaying pain, but so far as I know, no nurse has ever made a single contribution to anesthesia. In the hands of nurses, and in the hands of many physicians as well, anesthesia is a craft, a craft often beautifully perfected in some of its aspects, but not the part of medicine it might be. (The nurse anesthetist will be considered further, under the hospital's department.)

On the other hand, the first-rank problems of anesthesia are as fundamental, and as difficult, as any in medicine. The anesthesia process is inextricably bound up with irritability of tissue, one of the most fundamental characteristics of life. As Lillie pointed out years ago, the problem of the general nature of anesthesia is inseparable from the wider problem of the nature and conditions of irritability in general. Anesthesia, in its influence on cellular tissue, on the nervous system, provides an excellent tool for study of many physical and mental processes.

THE FUTURE

Some departments of hospitals carry a great burden of routine technical procedures. Examples are the departments of pathology, roentgenology, anesthesia. The routine work on these services cannot be cared for by volunteers as on the medical or surgical services where the volunteers' rewards are great. Insofar as one can look into the future, it seems probable that active *university* hospital departments of pathology and roentgenology and anesthesia will contain two distinctly different groups of men working side by side.

Men in one group will be attracted and held by large salaries, for which they will give up leisure and freedom of activity in their specialty. Men in this group will carry the burden of hospital routine in their respective fields. (Some of these men will also be valuable as teachers.)

In the other group men will have, ideally, freedom from routine duties, freedom to pursue whatever investigations they wish, with only enough routine work to keep serviceable their already mastered clinical technics. (This is essential if they are to speak with authority on clinical matters.) Their recompense will be not in salary, which will be low, at least during their developmental period, but their reward will come in freedom from overwhelming routine duties, in an environment where they can grow in intellectual stature and in academic achievement.

Unless anesthesia is taught in terms of principles, it can hardly rise above the status of a craft. The university cannot be expected to foster anesthesia based upon the standards of the clinic alone. Anesthesia must develop scholarly aims and standards, characteristics, of university caliber before it can expect the patronage of the university.

Great efforts are being made at this time to increase the prestige of anesthesia as a specialty, how successful these will be remains to be seen. Certainly, present accomplishments must be and will be more widely distributed in the future than at present. I am not speaking of this aspect. The present efforts to develop anesthesia as a specialty are too limited, so far, to improving the clinical side alone. Truly this has needed and still needs improvement. There can be no question about this. The efforts that are being made are of great importance, as far as they go. But a specialty that has poverty of intellectual interest can scarcely become mature. How can any field that leaves nothing for the imagination to dwell upon expect any but the dullest candidates? To attract good students, a specialty must offer more challenging matters than those dealing with judgment and technic alone, indispensable as these are to the conduct of good clinical work. Opportunities for intellectual adventures must be presented. Such opportunities are abundant in anesthesia. They need exploration.

II THE HARVARD UNIVERSITY-MASSACHUSETTS GENERAL HOSPITAL DEPARTMENT  
OF ANESTHESIA

Probably no two departments of anesthesia are or should be alike, but from the inquiries that are made concerning the principles and details of

organization of this one, an account of it may be useful, since it differs in many respects from the traditional. In several instances views that have been already expressed in the preceding section will be referred to here, even summarized briefly for clarity and for emphasis in the new context of this section.

#### PURPOSES

The Chief of the Department, as a Professor in Harvard University, has the obligation to teach and to do original work. As the Director of a Hospital Department he must provide the best possible anesthesia for the Hospital and carry on postgraduate training in clinical anesthesia. These fourfold activities will be discussed in detail, so also will the financial arrangements that make them possible. But first the principles that underlie the organization will be described. (There is some inevitable overlapping in the four categories mentioned.)

#### PRINCIPLES AND DETAILS RELATED TO INVESTIGATION IN THE UNIVERSITY'S DEPARTMENT OF ANESTHESIA

1 A great opportunity is afforded there to carry on studies in human pharmacology. A close association between the Professor of Anesthesia and the Professor of Pharmacology is desirable and an advantage to both. This should lead, not only to original work of distinction, but also to smooth clinical application of pharmacological and other basic advances. This requires judgment and insight of a high order. A close association between the clinic and the laboratory is essential if progress is to come.

2 It is the obligation of the University to choose as Professor of Anesthesia a man who is capable of doing original work of high quality. He must be provided with the time and equipment for work, and freedom from engulfing routine.

3 The chief intellectual stimulus in the field of anesthesia comes from investigation. For this reason, since a real intellectual challenge is necessary to attract good men, it is more important that the Professor of Anesthesia have the opportunity to carry on research than it is, say, for the Professor of Surgery. (The field of surgery is rich in resources and can attract good men for many reasons.) The chief hope of attracting good men to anesthesia as well as hope for growth of the field lies in investigation.

4 Anesthesia, in being relatively simple technically, fails to attract good men on this basis and is at the same time so baffling in its scientific aspects, as far as the mechanism of anesthesia goes that this also discourages good men. The only solution to this is further investigation. Anesthesia must attract those who are capable of original work, if it is to mature.

5 It is neither necessary nor desirable that all residents in anesthesia carry on so-called research. It is not only desirable but necessary that those

who are being fitted for an academic career do so. This presupposes that such men will have a plan for it.

6 Nurses have not contributed and cannot be expected to contribute to the development of anesthesia. (They work at a purely technical level, but so also do physicians who limit their interests to technics.)

#### PRINCIPLES AND DETAILS RELATED TO ACADEMIC TEACHING

1 It is desirable for the Professor of Anesthesia to lecture on the anesthetic agents in the medical school course in Pharmacology. He can thus stimulate the student's interest in the academic side of anesthesia in the second year of his medical course and can add clinical interest to this in the subsequent years of the student's training.

In the first three years of the medical course the student receives about 45 hours of instruction in anesthesia. This includes lectures, laboratory work, and firsthand administration of ether in the animal surgery courses. In the fourth year, weekly anesthesia discussion groups are held during the course in surgery. (Training of the student in clinical anesthesia on man is described in the following section on Clinical Teaching and Training.)

2 The Professor of Anesthesia must have available an abundance of clinical material for teaching and investigation and at the same time not be overwhelmed by routine clinical duties. Under our circumstances this requires that he function in the Medical School as a whole as far as teaching and research are concerned, but in *one* of the School Hospitals, as far as his clinical duties go, rather than in all. (This is customary at Harvard, and its counterpart can be seen in several departments, compare, for example, the Pathology Department.)

#### PRINCIPLES AND DETAILS RELATED TO CLINICAL TEACHING AND TRAINING

1 Anesthesia is not rich in technics, in the sense that surgery is. The technics of anesthesia are relatively simple. Probably few good men will ever be attracted to anesthesia by the technics alone.

2 The technics of anesthesia, like all medical procedures, are demanding in that even though once mastered they require constant application for continuing efficiency.

3 The technics of anesthesia require an apprenticeship type of training. Little is to be learned from observation alone, learning here, as in surgery, comes from doing. Therefore, it is necessary to provide an abundance of clinical material for use under guidance. Therefore, also, we struggle to avoid over-expansion of our training program, so that plenty of clinical material will be available for each man accepted for training. "Observers" are welcomed for a few days, a longer period passed in this way is probably a waste of their time.

4 Anesthesia technics must have a surer foundation than can be obtained in the clinic alone. It is important that they be taught in terms of principles first and details second.

5 The anesthetist should not be permitted to become a specialist without the broad clinical training in medicine required of other specialists in medicine

6 Men are trained for Board of Anesthesiology certification

7 Foreign students are accepted under rather stringent requirements (See below )

8 Interested medical students can take a month's course of fulltime training in anesthesia All medical students administer at least ten open ether anesthetics If they considerably exceed this number, they are taught to use nitrous oxide induction All sit with and chart the course of five patients under local or spinal anesthesia

9 It is desirable that house officers on the regular surgical service rotate through the anesthesia department, not to make anesthetists of them, but as a part of their surgical training so that they will understand the possibilities and limitations of anesthesia Most house officers spend two months fulltime on the Anesthesia Service

10 Nurses are trained to supply some needs Nurses are permitted to administer only ether anesthesia (nitrous oxide induction), and this because of its well demonstrated factor of safety (respiratory failure gives drastic warning of overdosage with check of intake of the drug before any circulatory damage occurs) An equal factor of safety is not present with other anesthetic agents, and nurses are not permitted to administer them

#### PRINCIPLES AND DETAILS RELATED TO HOSPITAL ORGANIZATION

1 The properly organized department of anesthesia should be self-supporting, and the department should pay its expenses (and it can if in the university hospital of average size about a quarter of the hospital beds are for private patients), but it should not make money Legitimate expenses are Salaries, supplies, equipment, a reasonable percentage payment for hospital overhead (bookkeeping, heating, light, janitor service, etc ) and a reasonable percentage of the income should be set aside for development of the department The department will not remain static It will go forward or backward, its continued development requires support If the department continues to make money after these things are adequately provided for, fees should be lowered

2 The Chief of the Department of Anesthesia must be free enough from routine obligations so that he can discharge the duties concerned with development of the department, teaching, and research This means he must have able associates who can relieve him of much of the routine work

3 The Hospital must provide the Professor of Anesthesia with abundant clinical material, for use as he needs it

4 Oxygen therapy and most other gas therapy should come under the supervision of the Department of Anesthesia Close interlocking arrangements with the Emergency Ward for resuscitation and with the Bronchoscopic Clinic for training of the anesthesia residents are necessary The anesthetist

should have charge of fluid therapy during surgery (When deterioration of the patient's condition occurs, the anesthetist informs the surgeon of it ) The anesthetist is an important member of various research groups in the hospital. He can lead at times, or follow at other times, but he is an integral part of investigation going on in the Hospital. The anesthetist must assume greater burdens than the clinical administration of anesthetic agents alone.

5 The able anesthetist who has spent as much time in preparing himself for his specialty as other members of the staff for theirs, deserves privileges and recompense equal to that of other staff members.

6 The costs of medical care are so great that anything that might cause them to rise (as, for example, the complete elimination of nurse anesthetists) must be examined with scrupulous care.

7 The final evaluation of drugs designed for use in man must in most cases be made in the clinic. The departmental organization must permit this (See principles related to investigation.)

8 Anesthesia is as closely related to surgery as asepsis or hemostasis. Separation of anesthesia and surgery, except for administrative, teaching, and developmental purposes, is unwise and not to the patient's good.

9 Men in the good positions of anesthesia are more of the same age than is true in the other specialties. There is a great shortage now of anesthetists. In future years this may be considerably less acute than now and departments organized on the basis of free help may, in the years to come, be in trouble, it being harder then than now to get good men good jobs with the result that fewer men will seek anesthesia training than now. (There will be many good opportunities again in 25 years.) The best anesthesia service can probably be provided by full-staff members with only a relatively few men in training, after the present great needs are filled.

10 Anesthetists are scarce, but even so the Anesthesia Department must be kept in balance in the Hospital as a whole, this chiefly concerns salaries, insofar as the great scarcity demand will permit.

#### DISCUSSION

In the preceding section on The Specialty of Anesthesia and in this section on Principles and Details, several of the items mentioned have either been discussed or do not need it. There are a few matters that perhaps need further elaboration. They will be taken up here.

*The Professor and the Clinic* We have in this University the situation in which the Medical School is associated with several hospitals. This raises the question of how, in certain specialized fields where only one professor can be maintained, this professor ought to spread his effort.

When a professor requires a clinical post, as he does in a clinical field like anesthesia, it must be in one of the school hospitals. It cannot well be in all. While he can function as a consultant to all, routine duties in all would destroy his usefulness. The primary responsibility of a full professor must always be to the university. Although he may serve well the hospital where he

is situated, the hospital is never his home in the sense that the school is. The hospital is the sea in which he swims and from which he brings up such treasure as he can. The professor working in a clinical field dare not cut himself off from this clinical material. It must always be available. It contains the source material of whatever contribution he can make to medicine. The clinical material must not possess him, but he the material, as he needs it, on his own terms.

When a professor's seat is in one institution, that institution must, in return for this advantage, free the man from entangling hospital obligations by providing able associates, supported by the hospital, to manage most of the routine work. The establishment of a strong department in one school hospital will inevitably strengthen those in other hospitals. New attitudes, new procedures, new standards, new principles will emerge from the one that can be used by all. The hospital where the professor is, profits. All of the hospitals profit. And the professor has clinical material to use as he needs it. Unshackled by routine, he must be free to develop his department, to carry on the research and teaching that are his first responsibilities.

The teaching responsibilities interlock the Hospital and the Medical School, for teaching in this field has two sides: (a) basic science (Department of Pharmacology, at the Medical School) and (b) clinical (Department of Surgery, at the Massachusetts General Hospital and at the Medical School). A very satisfactory arrangement has been worked out with the Professor of Pharmacology whereby the Professor of Anesthesia lectures in that Department on the Pharmacology of the Anesthetic Agents. Acquaintance is made with the entire second class of the Medical School, and this acquaintance is developed by later lectures and clinics in the Department of Surgery, and finally in the third and fourth years by voluntary and elective courses in clinical anesthesia. The Professor of Anesthesia functions, then, in two departments of the School, but inseparably in the Hospital as well.

These arrangements for anesthesia have been put into operation in the Harvard Medical School and the Massachusetts General Hospital. Both sides have carefully supported the concepts described here.

The Department is robustly supported by the Hospital, both Trustees and Staff, supported to such an extent that in the present postwar reorganization we are constantly extending the service. In the beginning, the obstacles were great and progress difficult. But now an opposite condition exists. With the shortage of ably trained men so great, the danger is over-expansion.

The University Hospital can develop either of two types of anesthesia department. (a) There is the one that prides itself on, and indeed often achieves, a high degree of technical excellence, but limits itself to this. This type of department can be built up rather easily, depending on how willing the institution is to pay for it. Men to head such a department are not difficult to find. Beyond its technical services such a department will have little influence on the hospital or school as a whole, and none on the specialty. (b) The second type can have not only the goal of technical excellence, but also a profound interest in the foundations of the field, in improvements in it.

of a basic kind, with a chief who will be considered as an equal by other departmental heads. Needless to say, such a man will be hard to find. Often the best solution for this problem is for the university to choose a young man who has the necessary qualities of mind and interest, and send him away for the necessary special anesthesia training.

*Hospital Interns, Residents and Fellows* Hospital interns in surgery, while on the anesthesia service, and residents and fellows in anesthesia operate under the direction of the anesthetist according to the following plan. House officers in general surgery are assigned to Anesthesia for two months as a step in their training. Emphasis is placed upon observation of the behavior of patients subjected to anesthesia and surgery, with the aim of impressing upon these men early in their careers, not only the problems and limitations of anesthesia, but its possibilities as well, as a part of good surgical care.

The Anesthesia Department contains 20 physicians. Four of these are fulltime in research and the others fulltime in clinical anesthesia. There are 11 nurse anesthetists, with 9 in training\*. A curriculum is provided for the training of physician anesthetists. A general internship of *at least* one year is required as a preliminary. Appointments are usually made for one or two years, but reappointments are made in suitable cases until the requirements are fulfilled for certification by the American Board of Anesthesiology.

In this course of training, increasing responsibility is given in the application of the various technics of anesthesia. Inhalation, intravenous, spinal, local and regional block. Training is provided in resuscitation, oxygen therapy and in bronchoscopy. Formal instruction is given in the pharmacology of anesthesia. Facilities are available for teaching and for basic and clinical research in the case of qualified individuals. Twice weekly, discussion groups and seminars are held. A close association with the Department of Surgery and the Department of Pharmacology of the Harvard Medical School is maintained.

Foreign students are carefully limited at the present time, owing to the great shortage of adequately trained men here. The occasional foreign student who is accepted for training comes on the following basis. For not less than one year, not more than two years. He must speak English well, and most important, he must be guaranteed a university teaching position to return to. Men who want training from even large foreign non-university hospitals are not accepted. We are convinced that these basic requirements help us to offer the most we can to foreign students and the lands from which they come.

*Financial Arrangements* The anesthesia department in the usual type of university hospital where private as well as ward patients are admitted, can be easily self-supporting.

In the present case about two-thirds of the Professor's salary comes from the University and one-third from the Hospital.

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\* Agitated discussion concerning nurse anesthetists is rarely heard in this Hospital. In about a dozen years the Massachusetts General Hospital has progressed from no physicians in anesthesia to 20 with maintenance of a group of nurses.



Charges to private patients for anesthesia are made so that with the lower surgical fees, the anesthesia charge is about 15 per cent of the surgical, and in the case of the higher surgical fees, about 10 per cent. The anesthetist is usually closer to the patient than the pathologist or roentgenologist. Possibly work by men in these two fields can be established on a set fee basis. Anesthesia charges should, like those of the surgeon, be scaled to the patient's ability to pay. This is arranged by placing the charges for anesthesia at a fixed percentage of those for surgery. However, in the case of ward patients, fixed anesthesia charges are made as follows: Five dollars for the first two hours, \$7.50 for three hours, and \$10 for procedures that last over three hours.

With the great shortage of physicians trained in anesthesia at the present time, an acute problem is to keep the income of anesthetists in proper balance with that of other physicians working in the hospital. The Chief of the Department can take an all-out partisan view and get all he can for the Anesthesia Department, without regard for the remainder of the Hospital's staff, since Anesthesia is an easy earner. Or he can try to keep a balance with the whole hospital. Or he can steer a middle course between these two approaches, since he will hardly be able to defy the law of supply and demand.

**DISCUSSION—DR FRANK H. LAHEY, Boston.** It would be wrong for this paper to go undiscussed because it is such a good paper and such an important subject. Even if approached from a more utilitarian point of view than that of the author, it is still an urgent subject and one that has been neglected by the universities. Interest in anesthesia until recently has been evidenced largely by those who have been dealing with the subject from a clinical point of view and we are now observing an interest from the investigative viewpoint, which will round out the subject as it should be.

Over the years we have been greatly interested in the problem of anesthesia because it is so closely related to our surgical problems. We have run a school of anesthesia for a number of years, except during the period of the war when practically all the men in this school were being trained for anesthesia in the Navy, 41 being made available for Navy service. This has been a two-year period of training and, when the men have completed it, they are capable of heading a department of anesthesia in any medical school or any hospital.

Up to the time of the war I feel certain there had been a great lack of appreciation of the value of a trained physician-anesthetist. Because so many surgeons were able to have trained physician-anesthetists in the war, this has been largely overcome. Prior to the war we had difficulty in placing the men whom we had trained in anesthesia in suitable positions but we now have a demand which far exceeds the number we can supply.

Trained anesthetists can supply so much today that it is of interest to enumerate what they should be able to do. They should be able to grade the risk. They should be able to advise surgeons in consultation as to the most desirable type of anesthesia for a particular operation. They often can make suggestions in a given problem case which will be of distinct value in the management of surgical procedure. They should be able to take complete charge of the patient's care on the table, which has been such a heavy responsibility up to recent years for an operating surgeon already seriously burdened with responsibility. They should be completely responsible for transfusions, with so many patients today requiring and receiving transfusions while under anesthesia—at which time the early symptoms of improper matching cannot be appreciated—this is a real responsibility since they are responsible also for the accuracy of blood matching. They will save cardiac patients in cardiac arrest at the time of operation. We have had twelve patients

with cardiac arrest (two of these had carotid sinus syndrome), of whom we have saved four with no subsequent cerebral damage. The heart was started in every case of the twelve, but too late to avoid cerebral changes in eight. Dr. Hamilton Bailey has recently reported an experience with 40 cases of cardiac arrest. The responsibility to restore cardiac action in patients with cardiac arrest is completely in the hands of the anesthetist, since he will be the one who first discovers it, and his acuteness and promptness in this respect will settle whether or not the patient lives. The anesthetist will be the one who will deal with carotid sinus reflexes, of which we have had several instances. One has to have only a few such cases to realize how hair-raising they are. The anesthetist will be responsible for shock, he will not permit the patient's blood pressure to drop and remain low over any period of time. In the early days before we had such good anesthesia and also improved surgery, our patients after operations of major magnitude usually left the table cold, blue and wet. Today, as a result of the excellent care competent anesthetists provide for them on the table, together with good anesthesia, and in spite of very extensive procedures, they now leave the operating room warm, dry and pink. This is purely the result of the responsibility for their condition being in the hands of the anesthetists. They should be able to provide diagnostic blocks. They should be able to do bronchoscopies, to handle 100 per cent oxygen, helium, and any number of things that only add emphasis to what I have already stated.

As to the supply side of the problem, there are not and will not be enough professional anesthetists to go around unless we do more than we are doing in training anesthetists in the various hospitals. Every hospital that takes on a professional anesthetist has, in my opinion, a serious obligation to see that he, in turn, is training other anesthetists.

As to the effect of this expert anesthesia upon surgery itself, I have repeatedly said that in my opinion it has definitely decreased the morbidity and mortality, and I would like to emphasize further that a good professional anesthetist will lower the morbidity and mortality in the surgeons themselves.

DR. ALFRED BLALOCK, Baltimore. I rise mainly to express my admiration for the author of this paper and the guest of this Association, Dr. Beecher. His work in the field of anesthesia has done much to advance this subject. He is a leader in research, in the teaching of students and in the training of anesthetists. Dr. Beecher does not advocate that anesthesia be divorced from surgery. In fact, he states that anesthesia and surgery are bound to each other as are surgery and hemostasis.

I am alarmed by the present tendency of some to discredit the ability of the nurse-anesthetist. All of us must be aware of the damage that may result from articles in the public press to the effect that it is unsafe to be operated upon in a hospital which is not staffed solely by physician-anesthetists. Furthermore, is it proper to maintain that the nurse anesthetist is only a technician? There are hundreds of hospitals in this country in which major surgery is performed and the number of M.D. anesthetists is totally inadequate to staff these. Even if it is desirable that these positions should be filled only by physicians, I doubt seriously if this field of work will attract physicians in sufficient numbers to supply the need within the next few decades. Conversations with a number of physician-anesthetists lead me to believe that many of them deplore the present inclination of some members of the profession to underrate the ability and the worth of the well-trained nurse-anesthetists. Many of these have exceptional qualifications. For example, Miss Olive Berger has anesthetized the last 225 patients upon whom I have operated for congenital heart disease, and my associates and I have the highest regard for her ability.

We are fortunate in having heard Dr. Beecher, whose general ideas regarding the field of anesthesia are sound and commendable.

## GRADUATE TRAINING IN SURGERY IN VETERANS ADMINISTRATION HOSPITALS\*

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THE RETURN FROM MILITARY SERVICE to civilian life of many thousands of medical officers whose training was interrupted by the war and who desired to complete specialty qualifications created a problem far beyond the scope of existing graduate educational facilities. The medical care of veterans of both World Wars in facilities which had been inadequate to meet the needs of World War I alone, created a problem for the Veterans Administration which would have been insurmountable under former methods of administration. Under the direction of General Omar Bradley, the reorganization of the Veterans Administration hospital program by Dr Paul Hawley, with the assistance of Dr Paul Magnuson, has progressed far beyond expectations in meeting these two problems. The prime purpose of their program is to offer the best available medical care to men and women who have served their country in the Armed Forces. Any program which would not fulfill this purpose would not be justifiable. Yet facilities and personnel available to them when they assumed their present responsibilities were so inadequate to meet the needs of veterans of World War I alone that most existing hospitals had long waiting lists and an insufficient number of physicians to render prompt medical care. They knew that existing opportunities in the Veterans Administration would not attract the number of competent doctors required to meet the expanding needs. Their vision in enlisting the aid of medical schools has to a large extent solved these problems. It has made available to the veteran patient the faculties of participating medical schools and thus some of the finest medical talent in the country. It has given to the most promising veteran medical officers an opportunity to complete their training and at the same time render valuable medical care to men who have become afflicted with disease during or subsequent to military service.

Briefly, the professional care of patients in veterans' facilities located near universities has been placed under the supervision of medical schools able and willing to participate in the program. Committees composed of deans of these schools have assumed responsibility for the successful accomplishment of these aims. The wholehearted support of medical schools throughout the country is shown by the following table enumerating the number of such programs now in operation.

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\* Read before the American Surgical Association, March 25, 1947, Hot Springs, Va.

† Deputy Chief, Surgical Service, Veterans Administration Hospital, Hines, Illinois.

GRADUATE SURGICAL TRAINING

TABLE I  
VETERANS ADMINISTRATION RESIDENCY TRAINING PROGRAMS  
(as of February 1, 1947)

Medical schools participating	55
Deans' Committees Supervising	33
VA hospitals and clinics utilized	58
Residents in training	1 635

Good civilian hospitals long have recognized the importance of internes, residents or both in rendering the best professional care to patients. All teaching and superior private or municipally administered hospitals depend upon an adequate house staff to maintain high professional standards. By establishing residencies in Veterans Administration hospitals, nearly 2,000 competent young physicians are now helping to meet the demands of the veteran patient and at the same time are furthering their training under supervision of the country's best medical educators. Many of these men, who otherwise would not have been attracted to this service, will make a life work of it and assure continued good care in Veterans Administration hospitals.

As the specialty boards have set up standards recognized as essential to the training of qualified specialists, their requirements have been used as the basis for resident training programs established by the Deans' Committees and the Veterans Administration. In spite of the short time that has elapsed since these programs have been introduced, many already have been approved and many more are awaiting inspection.

TABLE II  
SPECIALTY TRAINING PROGRAMS IN VETERANS ADMINISTRATION HOSPITALS  
Approved by Council on Medical Education and Licensure of the American Medical Association

Association	52
Applications for approval	129
Approved by the American College of Surgeons (Many awaiting inspection for approval)	59

One of the first Deans' Committee programs was instituted at the Veterans Administration Hospital at Hines, Illinois, under supervision of the Colleges of Medicine of Northwestern University and the University of Illinois. This program will be discussed somewhat in detail to exemplify what has been established and what has been accomplished in the first year under the present administration. Although Vaughan General Hospital, formerly administered by the Army Medical Corps, has been utilized as an addition to the Veterans Hospital, almost its entire capacity is being used for the care of paraplegic, tuberculous, psychiatric and neurologic patients. After the reduction of overcrowding by the elimination of hundreds of emergency beds, the actual capacity for general medical and surgical patients at Hines has been

TABLE III  
ADMISSIONS TO VETERANS ADMINISTRATION HOSPITAL HINES, ILLINOIS

	Total		Monthly Average
1945	11 118	1945	926
1946	17,748	1946	1 479

increased by less than two hundred beds. Thus the increase in patient admissions is far greater than would be expected from the increase in bed capacity.

This increase in admissions is due largely to an acceleration in the care of patients enabled by a more adequate professional staff. The former staff worked efficiently but was so inadequate in number that it could not maintain a rapid turnover of patients. Many bottlenecks existed because of insufficient equipment and personnel. Many of these have been corrected but others still exist which must be eliminated before the hospital can function at maximum efficiency. When contemplated changes are completed, each hospital bed will serve at least twice the number of patients it formerly did. The greatest present handicap is a shortage of operating rooms. Only five operating rooms are now available to serve nearly a thousand surgical beds. As a result, the hospital stay of many patients is prolonged by at least one to two weeks awaiting operating facilities. In spite of this, the admission of surgical patients has been nearly doubled.

TABLE IV

ADMISSIONS TO SURGICAL SERVICE VETERANS ADMINISTRATION HOSPITAL HINES ILLINOIS

	1945	1946
General Surgery	1 250	4 130
Tumor Service	2 344	2 359
Orthopedic Surgery	637	1 401
Urology	697	1 184
Women's Surgery	227	286
Eye ear nose and throat	537	1 289
Total	5 692	10 649

By utilizing the operating rooms both morning and afternoon on a closely integrated schedule, the number of surgical procedures performed in the existing facilities has now greatly increased.

TABLE V

OPERATIONS PERFORMED AT VETERANS ADMINISTRATION HOSPITAL HINES ILLINOIS

Specialty	1945	1946	Increase	%
General Surgery	2 391	3 829	1 438	60
Orthopedic Surgery	337	699	362	107
Plastic Surgery	214	457	243	114
Urologic surgery	471	884	413	88
Vascular surgery	206	343	137	67
Thoracic surgery	279	375	96	34
Neurosurgery	87	318	231	265
Total	3 985	6 905	2 920	73%

However, no attending surgeon can be permitted to operate more than two half days per week because of this shortage of space. Plans are completed to construct more operating rooms which should increase the surgical output by at least 50 per cent. A separate operating room exists for the ophthalmologic and otolaryngologic services. These have been active services in the

past, but their reorganization has been considerably delayed. Operations performed on these services are as follows:

	1945	1946	Increase	%
Ophthalmology	141	284	143	101
Otolaryngology	1,083	1,140	57	5

An additional operating room has been completed for these specialties and its benefits are being reflected in their present output.

#### PROFESSIONAL STAFF OF VETERANS ADMINISTRATION HOSPITALS

Four categories of physicians now serve the veteran patient. They are:

- 1 Consultants
- 2 Attending physicians and surgeons
- 3 Full time Veterans Administration physicians
- 4 Residents

The consultants are outstanding specialists whose services are sought when professional problems arise which cannot adequately be met by the attending staff. They also serve in an advisory capacity in the administration of many special departments. The attending physicians and surgeons are responsible for the professional care of a great majority of veteran patients. These men spend an average of five half days per week in carrying out their duties. They must be veterans of World War II, faculty members of a sponsoring university, and must be certified by a specialty board or have equivalent training. A few full-time Veterans Administration physicians are included on the professional staff of some of the Deans' Committee hospitals. Their services are very valuable in handling the administrative work required by the Veterans Administration and in helping to maintain satisfactory function of the various departments. Thus far all residents are veterans who have been in active service during World War II. As internes are not utilized at present, it is the resident's responsibility to take case histories and physical examinations and to request all necessary special studies demanded for an accurate diagnosis. On the surgical services, they are responsible for the pre- and postoperative care of patients assigned to them. They assist the attending surgeon at all operations and perform those operations under the direction of the attending surgeon which he believes them competent to perform. The residents are most important in the efficient functioning of the hospital's professional staff. The number appointed is determined by the hospital's needs. It is our opinion that one resident cannot satisfactorily handle more than 20 to 40 patients, the number varying with the type of service to which he is assigned. In general surgery, one resident is responsible for 30 patients. In some of the specialties, a smaller number of patients is assigned to each man, whereas in others the number can be increased. However, in order to meet training requirements, it is necessary to assign residents to basic science studies and to other hospital functions. On the surgical service at Hines Hospital, an over-all ratio of one resident to 18

patients has enabled us to meet hospital requirements and training needs. At present we have 144 residents who are distributed as follows:

TABLE VI

Internal medicine	44
Neurology	7
Psychiatry	6
Surgery	
General	41
Orthopedics	8
Urology	7
Thoracic	3
Neurosurgery	4
Otolaryngology	4
Ophthalmology	3
Anesthesiology	11
Radiology	6
Total	144

## RESIDENT TRAINING PROGRAM

The requirements for resident training have been fairly well established by the specialty boards. These requirements, with some modification, are used as our criteria for our own training program. A few principles have been incorporated by the Deans' Committee to somewhat amplify this program. They believe that a man trained in any surgical specialty must have a broad foundation in the principles of general surgery and in the basic sciences. For this reason, men being trained in surgical specialties are required to spend six months on the pathologic service where they are trained in both pathology and in surgical anatomy. From six to 18 months are spent on general surgical services. After completion of this training, the men then are assigned to services in their own chosen field.

Likewise, it is believed that some knowledge of surgical specialties is important to the development of a competent general surgeon. Although the program varies to some degree with the desires of the individual resident, the following outline includes those services through which most general surgical residents rotate:

TABLE VII

## PROGRAM FOR GENERAL SURGICAL RESIDENTS

	Months
Admitting service and night surgery	3
Tumor diagnosis and therapy	3
Surgical specialties (four of 3 months each)	12
General surgery	12 to 18
Pathology and anatomy	6
Other basic sciences throughout entire residency	

*Admitting Service.* When the Deans' Committee assumed responsibility for the professional care of patients at the Veterans Administration Hospital, Hines, Illinois, a survey was made to determine how many hospitalized patients actually needed hospital care. It was found that nearly 40 per cent of patients in the hospital could be treated satisfactorily as outpatients or could not be benefited by further hospitalization. These patients occupied a

sufficient number of beds to make it impossible for existing facilities to meet the veteran hospital needs of the community. At that time, admissions to the hospital were accomplished by full-time physicians who did not participate in the professional care of patients and who were less concerned with the dangers of overcrowding and with the ability of the hospital to meet the demands placed upon it than were physicians who were actually serving in the hospital. As a result a waiting list of nearly 2,000 patients existed in the early part of 1946. This included veterans suffering with malignant disease upon whom action had been deferred for several months. Many patients upon whom elective surgery was indicated were required to wait as long as one year before they could be hospitalized. This often meant prolonged unemployment if correctible diseases prevented occupation. It was believed that more careful screening of patients for admission would enable the hospital better to meet the community demands. As the residents are competent to recognize disease and are conscientious in admitting only patients who need hospitalization, a number are assigned to the admitting service where they take histories and examine all patients applying for admission. If any question of doubt arises, consultation is called and utmost care is taken not to refuse hospitalization to any patient whom it would benefit. By the use of this system, although more than 50 per cent of people applying for hospital admission are rejected, we know of no instances where care has been denied to any patient needing hospitalization. This careful screening has not only enabled the hospital to meet the community needs but it has also entirely absorbed the waiting list, and all veterans applying for admission can be immediately admitted to the hospital when such service is needed. This is true in spite of the fact that the hospital is now serving not only World War I veterans but also those of World War II. During 1945, more than 90 per cent of hospitalized veterans had served in World War I. At present over 60 per cent of patients are veterans of World War II. This indicates that the number of veterans being served by the hospital has more than doubled. Thus by careful screening of patients and by nearly doubling hospital admissions, existing facilities are now serving a function three to four times as great as they did two years ago.

Each surgical resident spends six weeks on the admitting service. He is not assigned to this service until he is sufficiently familiar with hospital routine to understand the importance of his duties and is sufficiently trained to perform these duties in a highly satisfactory manner. While on this assignment the resident does not have actual operating room service but he receives experience in diagnosis which is important in the training of a surgeon.

*Night Surgery* Because most Veterans Administration hospitals do not have facilities for housing residents and as many of them live at considerable distances from the hospital, it is impracticable for them to be subject to call both day and night. For this reason, a night service has been established to which each surgical resident is assigned for a period of six weeks. He is available for any calls on the surgical wards and for the care of emergency surgical admissions. A senior surgical resident is on night duty at all times to assure



competent surgical judgment. When he deems it advisable, he solicits the aid of an attending surgeon.

*Tumor Diagnosis and Therapy.* Training in the recognition and institution of proper therapy of malignant disease is essential to every surgeon. As nearly 2500 patients suffering from some form of cancer are admitted to the Veterans Administration Hospital, Hines, Illinois, an excellent opportunity for training in this field is available. Although patients with surgical tumors are assigned to the specialty in which field the lesion is located, all tumor patients are seen in consultation by the tumor service and are reviewed by the tumor board. After appropriate therapy and before discharge from the hospital, these patients again are presented before the tumor board. This vast experience is invaluable to the surgical residents who are assigned to the tumor service for a minimum of three months. As the chief of the tumor service is a well-trained oncologist and has had special training in surgery for malignant disease of the head and neck, the surgical ward for such lesions is a part of the tumor service. Non-surgical tumors which are treated by radiation also are hospitalized on this service. Although it is not our desire to train surgical residents to become radiologists, we believe it important for them to be cognizant of the possibilities of this form of therapy.

*Basic Sciences.* Considerable controversy exists as to whether basic sciences, particularly pathology and anatomy, should be taught on a full-time basis covering a period of weeks or months or should be incorporated with clinical teaching throughout the residency period. Theoretically, the latter has some advantages. However, experience has shown that residents on active clinical services frequently do not allow sufficient time for basic science study. Because of the excellent teachers and the amount of material available to us in the basic sciences, we have adopted the policy of assigning each surgical resident to the pathologic service for a period of six months. The comprehensive course of lectures by the chief pathologist and attending pathologists from the faculties of the sponsoring medical colleges provides excellent training in the study of abnormal tissues. The large number of surgical specimens and the great amount of necropsy material offer unusual teaching opportunities. During this period of six months, surgical anatomy is taught on available material by an anatomist who is also certified by the American Board of Surgery and who lectures and demonstrates from a surgical viewpoint. Sufficient time is available to the resident during this six months' assignment for him to complete or become well established upon a clinical or pathologic research problem. Excellent library facilities are at his disposal to encourage complete review of pertinent literature. Other basic sciences, particularly bacteriology, physiology and bio-chemistry are taught at weekly conferences throughout the entire residency. In these conferences stress is laid upon the clinical application of the basic sciences.

#### ALLIED SPECIALTIES

*Roentgenology.* In order to give surgical residents a better understanding of roentgenology, weekly conferences are held in this subject. In addition to

this, the staff and consulting radiologists are available at all times to review with the residents roentgenograms and fluoroscopic studies of their patients

*Anesthesiology* The department of anesthesiology is administered as a subdivision of the department of surgery. Only graduate physicians are used as anesthetists. Four physicians certified by the American Board of Anesthesiology supervise the work of 12 residents in this department. The residents in anesthesiology examine all patients prior to operation and cooperate on pre-operative orders and the selection of anesthetic agents. They are equally responsible with the surgical resident for the care of postoperative complications, especially those which may in any way be related to the anesthetic agent employed. Although surgical residents are not employed at present in the department of anesthesiology, it is believed that some knowledge in this field would be of benefit to them in their future careers as surgeons.

#### SUMMARY

The Veterans Administration hospitals will be called upon to serve 15 to 20 million former members of the armed forces. This is four times as great a number as they served prior to World War II. Although expansion of existing hospitals and construction of new ones will be necessary and are contemplated to meet this demand, it will be many years before such construction can be completed. It has been shown that by proper administration and with adequate personnel, existing hospital facilities of the Veterans Administration can serve a far greater purpose than they have in the past. They not only can offer better and more extensive medical care to the veteran patient, but can provide excellent graduate training facilities for the returned medical officer. The Veterans Administration has solicited the aid of the medical schools of this country to help in this program. It is the responsibility of the participating Deans' Committees to so organize the professional services of the hospitals that they will render the best possible professional service to the veteran patient and offer the greatest possible training opportunities in the surgical specialties. It is also their responsibility to the taxpayers of the country to supervise the professional care in these hospitals in such a manner that undue expansion will not be necessitated by inefficient administration.

DISCUSSION—DR PAUL B. MAGNUSON, Chicago. The medical profession has supported this program from the start and I think has accomplished something never before even dreamed of in any country. We did not know when we started what co-operation we would have from the medical profession, and I doubt that we would have had this whole-hearted support had not General Bradley and General Hawley authorized the plan to set up Veterans Hospitals on the basis of mutual advantage. This advantage, I believe, is apparent to all who are teaching.

In the first place, we had to take care of the veteran patient. Second, we were under obligation to provide the veteran physician with further training in view of his having been called away from training to serve in the armed forces. The 1600 Residences created in about a year are serving to continue training for those men whose careers were interrupted by the war. These Residents have been paid more than will be the case in the future when Residents will not be veterans. The sum of \$3300 is a lot to pay a Resident, but the Senior Resident's pay of \$1800 was supplemented, because under the Bill of

Rights these men were entitled to up to \$500 per year for educational purposes, plus \$65 per month if single and \$90 if married, for subsistence. Taking into consideration the fact that they were all older men, many of them married, it was felt that they were entitled to a greater compensation on their return from service, therefore their pay was placed at a higher figure than it will be in the future.

We also owed another debt to men coming back from service, men well trained and working in universities, who were called into service before they had the opportunity to become established, men coming back who had neither offices nor practices. By offering the schools the advantage of putting these men in part time positions, giving service to veterans at a reasonable compensation while building up their practices, we helped that group.

The older group, most of us, stayed home, we were too old or too decrepit to go into the army, according to General Kirk's standards. This group, largely men of professorial rank, has guided the program through with the assistance of the Deans' Committees of all the medical schools. The Deans' Committees chose to act without compensation because by so doing they would not be under pressure from any source. This has been of mutual advantage, for this reason. The promising young men as they finish their Residencies can retain affiliation with the medical school, can be put on as attending men at Veterans Hospitals, and at the same time can continue with research and laboratory work until such time as the medical school decides whether or not they want them on the faculty. Most medical schools do not have the funds to retain such men at any stipend.

Most of the new hospitals will be built on the campuses of universities. They will not be domiciliary hospitals, they will be hospitals for acute care. Fort Snelling at Minneapolis cut the hospital stay from 42 bed days per patient to 19 bed days per patient, and I think that would compare favorably with most civilian hospitals.

The medical profession must retain control of this program or, as Dr. Puestow said, it will go back into the same old hands. We must have strong men, not only in the hospitals controlled by the Deans' Committees but in Washington and in the various districts. It is up to the medical profession to hold the ball, now that they have it, and run with it. If we do not—well, politicians and bureaucrats live on for ever!

DR. EDWARD D. CHURCHILL, Boston. I should like to ask Dr. Magnuson why, if this group of young men is going to save the country thirty billion dollars and carry this work load—why decrease their salaries?

DR. PAUL B. MACNUSON, Chicago. If we were to go into a city where the ordinary stipend of a Resident is \$1200 a year, and offered \$1800, \$2400, \$3000, we would be putting our Residencies in competition with Residencies in universities that are assisting in this training program. We do not intend to put the same value on service in communities where it costs fifty cents on the dollar to live—if any such exist—in comparison with cities where the expenses are much higher. The cost of living in a small community is much less than in Chicago or New York, or the other robber baron eastern cities. We feel compensation for Residents in the Veterans Administration should be equalized with that of civilian hospitals. Certainly we did not want to put these Residency appointments on a competitive basis of money alone, because we might get Residents who were more interested in dollars and cents than in the training offered. Therefore, in the future they will be offered the same compensation as is prevalent locally, according to their grade—junior, intermediate or senior.

# TOXOID IMMUNIZATION IN EXPERIMENTAL GAS GANGRENE\*

## A Preliminary Report

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THUS FAR EFFECTIVE PROPHYLAXIS in gas gangrene has been limited to early and adequate surgery.<sup>1,9</sup> Recently penicillin, administered parenterally,<sup>10</sup> has been shown to be a very valuable therapeutic adjunct to surgery. Its prophylactic effect was greatest when it was used early and in massive doses and consisted of a limitation of the rate of spread and extensiveness of the infectious process as well as a marked retardation in the rate of death.

The possibility of producing active and effective immunity for this infection has been explored in recent years, since various powerful exotoxins generated by the clostridia play an important role in the pathogenesis and toxemia of gas gangrene. Kolmer<sup>11</sup> studied the immunizing capacity of the toxoids of *Cl welchii*, *Cl septicum*, and *Cl oedematiens* in guinea pigs and concluded that the degree of acquired immunity was much less than that produced by tetanus toxoid. Stewart<sup>12</sup> also investigated the effect of two injections of *Cl welchii* toxoid in guinea pigs and found that the animals which developed titers of 0.25 or more units of antitoxin per cc showed marked resistance to intramuscular inoculations of either toxin or virulent cultures. Robertson and Keppie<sup>13</sup> confirmed the observations of Stewart on serum antitoxin levels necessary for protection against lethal doses of bacteria. Dowdy<sup>14</sup> working with single doses of *Cl welchii* toxoid in dogs, reported in 1945 that 0.1 unit per cc of serum of alpha antitoxin was the critical level determining the survival of dogs challenged with intramuscular injections of virulent cultures. In a group of 23 dogs with serum titers less than 0.1 unit per cc there was a 43.5 per cent survival rate, whereas in a group of 51 dogs with serum titers of more than 0.1 unit of antitoxin per cc, there was a survival of 96 per cent. When he gave an additional or booster dose of toxoid, he obtained a marked increase in the serum antitoxin titer and a survival rate of 100 per cent.

Logan and Tytell<sup>15</sup> compared data on the immunologic response of animals to various *Cl welchii* toxoids and came to the same conclusions as Dowdy. They prepared an alum precipitated *Cl welchii* toxoid which was found to be effective in producing a measurable and protective titer of antibodies in mice, guinea pigs, rabbits, pigeons, dogs, and humans. Good protection was obtained in the animals against multiple lethal doses of toxin and bacterial cultures injected into healthy muscle through fine needles.

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\* Read before the American Surgical Association, March 26, 1947, Hot Springs, Va

These studies were very interesting but from a surgical point of view several criticisms became obvious. The experimental lesions produced by the injection of toxin or virulent bacteria into healthy muscle are vastly different from those of clinical gas gangrene, which are almost invariably associated with large areas of grossly contaminated and devitalized tissues, produced directly by trauma or indirectly by laceration or thrombosis of nutrient arteries. In addition, experimental gas gangrene produced by the simple injection of toxins or bacteria is much less severe<sup>10, 16</sup> and more responsive to therapy than that produced in the presence of crushed muscle and dirt. Likewise, the use of local irritants such as calcium chloride along with the injected bacteria failed to produce as severe an infection. Furthermore, there is increasing evidence that the toxemia of gas gangrene is complex, being caused not only by the known bacterial exotoxins absorbed from the site of injury, but also by other factors, possibly arising from the septic degeneration of devitalized tissue. Consequently, it seemed probable that the immunity reported thus far in experimental animals injected with toxoid inadvertently has been made to appear greater than it really was. Finally, the inference that measurable amounts of antitoxin such as 0.1 to 0.25 units per cc. in the blood of patients or animals are necessarily synonymous with actual protection against a severe form of challenge or clinical infection has not been proved.

The problem of toxoid immunization against a more severe form of gas gangrene closely simulating the clinical type was undertaken in March 1945 through the combined efforts of the Departments of Surgery and Biological Chemistry of the University of Cincinnati, in an effort to evaluate fully the degree of immunity produced in experimental animals by injections of toxoid as advocated by Logan and Tytell, and to explore further the possibilities of effective immunity of experimental animals by other forms of toxoid prophylaxis.

#### MATERIAL

Guinea pigs were chosen as the experimental animal because of their marked susceptibility to *Cl welchii* infections and their immunological response which resembles closely that of the human being. In addition, most of the earlier work was done with this animal. *Cl welchii* was chosen as the test organism because of its occurrence alone or in association with other bacteria in 56 to 100 per cent of the cases of gas gangrene in a previously reported series<sup>17</sup>. Strain BP6K was used and cultures of it which were grown in pancreatic digest media were characterized by prolific growth with much turbidity and gas formation and a higher degree of virulence than those grown in deep meat broth, brain broth, or other media. When incubated for only 4½ to 5½ hours in the pancreatic digest media, they produced death in much higher dilutions than when incubated 18 to 24 hours. Weekly passage through pigeons was necessary to maintain the virulence at a high level and this was done routinely by the Department of Biological Chemistry. It was therefore possible to maintain the virulence of a strain of *Cl welchii* at a high level by incubating

for 4½ to 5½ hours in pancreatic digest medium a culture of BP6K passed weekly through a pigeon. The *Cl welchii* toxoid was produced from toxins of high potency and was made in large quantities by a reproducible procedure yielding many thousands of doses<sup>18</sup>. Concentration and detoxification was accomplished by precipitation first with ammonium sulphate and then with alum.

#### METHOD

Sixteen groups of guinea pigs consisting of 17 to 29 animals each received two or three injections of the alum precipitated toxoid prepared by Logan's method at varying intervals and with varying doses (Table I). A total of 364 animals were injected with toxoid and compared with 274 controls.

TABLE I

Group	No of Animals	Injection	Dose of Toxoid in Lb	Time of Injections Before Challenge in Weeks	Per Cent Survival
7B	17	2	30-30	28-22	12
12A	24	2	30-30	4-2½	33
15	25	2	30-30	8-3	100
12B	23	3	30-30-30	10-7-4	63
13	23	2	30-30	8-3	56
14A	25	2	60-60	7-4	70
16A	25	3	40-40-40	22-10-1-3/7	95
16B	25	3	40-40-40	24-20-1-3/7	60
16C	24	3	40-40-40	26-22-1-6/7	50
16D	29	3	40-40-40	28-24-1-3/7	24
17A	25	3	60-60-30	13-9-1-3/7	23
17B	25	3	60-60-30	14-10-1-3/7	65
17D	15	3	60-60-30	16-12-3-3/7	46
17-DT	15	3	60-60-30	16-12-3-3/7	26
18A	21	2	60-60	5½-2½	28
19	23	2	120-120	4½-2½	52
Controls	274			...	00 0

Seven groups received a series of two injections and nine received three injections. The individual doses of toxoid varied between 30 to 120 Lbs. The injections were made subcutaneously at varying times in an effort to determine the optimum intervals between inoculations. After expiration of the selected period of immunization, the groups were challenged by a severe form of experimental gas gangrene produced by the following method.

The skin over the lower back, posterior and lateral aspects of the thigh of a guinea pig was prepared by shaving and scrubbing with soap and water for five minutes. After the induction of drop ether anesthesia, the preparation of the operative area was completed by the application of alcohol, ether, and tincture of iodine. A sterile drape containing a hole 15 by 10 cm was then applied to the prepared area. These steps were necessary to eliminate or minimize the introduction of *Cl welchii* spores normally resident on the skin or hair of the guinea pig<sup>19</sup>. Under aseptic precautions using gown, gloves, cap and mask, an incision 10 cm in length was made through the skin and sub-

\* From the Department of Surgery, University of Cincinnati. The work described in this paper was done under contracts recommended by the Committee on Medical Research of the Office of Scientific Research and Development, the U. S. Public Health Service, and the U. S. Army.

cutaneous tissues over the mid portion of the postero-lateral aspect of the right thigh and developed down to and beyond the femur. The muscles on each side of the wound were then crushed five times with a Kocher clamp and then avulsed by twisting the clamp  $180^\circ$ . In each wound 0.5 cc (0.6 Gm) of an autoclaved and finely divided mixture of soil and cinders was placed. The edges of the wound were then closed with interrupted fine black silk sutures to minimize leakage of the inoculum and subsequent secondary contamination. In a previous series of experiments,<sup>16</sup> it had been determined that the presence of crushed muscle and dirt increased the virulence of *Cl welchii* 1,000,000 times. Serial dilutions of a  $4\frac{1}{2}$ – $5\frac{1}{2}$  hour culture of *Cl welchii* were then made to the tenth power using sterile pancreatic digest media as the diluent since it gave more uniform results than saline. Finally 0.5 cc of one of the higher dilutions representing 1–100,000 minimum lethal doses was injected through the skin into the operative area containing crushed muscle and dirt by means of a 25-gauge needle and a tuberculin syringe. The minimum lethal dose was considered to be 0.5 cc of the highest dilution of the culture which killed all of the guinea pigs within  $4\frac{2}{3}$  days under the conditions of the experiment on a given day.

Since the minimum lethal dose varied between a dilution of  $10^6$  and  $10^9$ , it was found necessary to control carefully each experiment by a group of 25 animals which were used to determine the minimum lethal dose on the day of challenge and under the specified conditions. This was done by the injection of 0.5 cc of serial dilutions of a  $4\frac{1}{2}$ – $5\frac{1}{2}$  hour culture of *Cl welchii* made to the tenth power from  $10^5$  to  $10^9$ . After challenge, the animals and their wounds were carefully observed over a  $4\frac{2}{3}$  day period, and the date of death and extent of the lesion were determined in each instance. In this manner it was possible to determine the minimum lethal dose for each experiment and to measure the degree of immunity produced by the toxoid injections against a severe form of experimental gas gangrene resembling closely the clinical type. Determinations of the blood titers of alpha antitoxin were made in 4 to 8 representative animals in each group to determine any correlation between actual immunity and antitoxin levels. All surviving animals were observed for an additional ten days. No other form of therapy or prophylaxis was used in these experiments.

### RESULTS

The degree of immunity obtained was found to vary between 12 per cent and 100 per cent, as measured by the rate and per cent of survival, depending on the number of injections, the size of the dose of toxoid, the interval between injections, and the severity of challenge.

When two injections of 30 Lbs of *Cl welchii* toxoid were given (Group 7B) seven months and  $5\frac{1}{2}$  months before challenge with 10–10,000 MLD's of *Cl welchii* culture, only 12 per cent of the animals survived the test period of  $4\frac{2}{3}$  days and all of the animals died within six days with extensive lesions (Fig 1 and 2). When the injections with the same dose of toxoid were

made two months and three weeks before challenge (Group 15) with 1-10,000 MLDs, 100 per cent of the animals survived for nine days, and 64 per cent were still living 15 days after challenge. The lesions produced in this group of immunized animals were minimal or definitely less severe and extensive than those in the control group. When the period of immunization was further shortened giving the same dose of toxoid in two injections four weeks and 2½ weeks before similar challenge, the results were not as good and only 33 per cent of the animals survived the test period of 4½ days (Fig 1). Likewise the lesions produced were more severe and extensive than in Group 15.

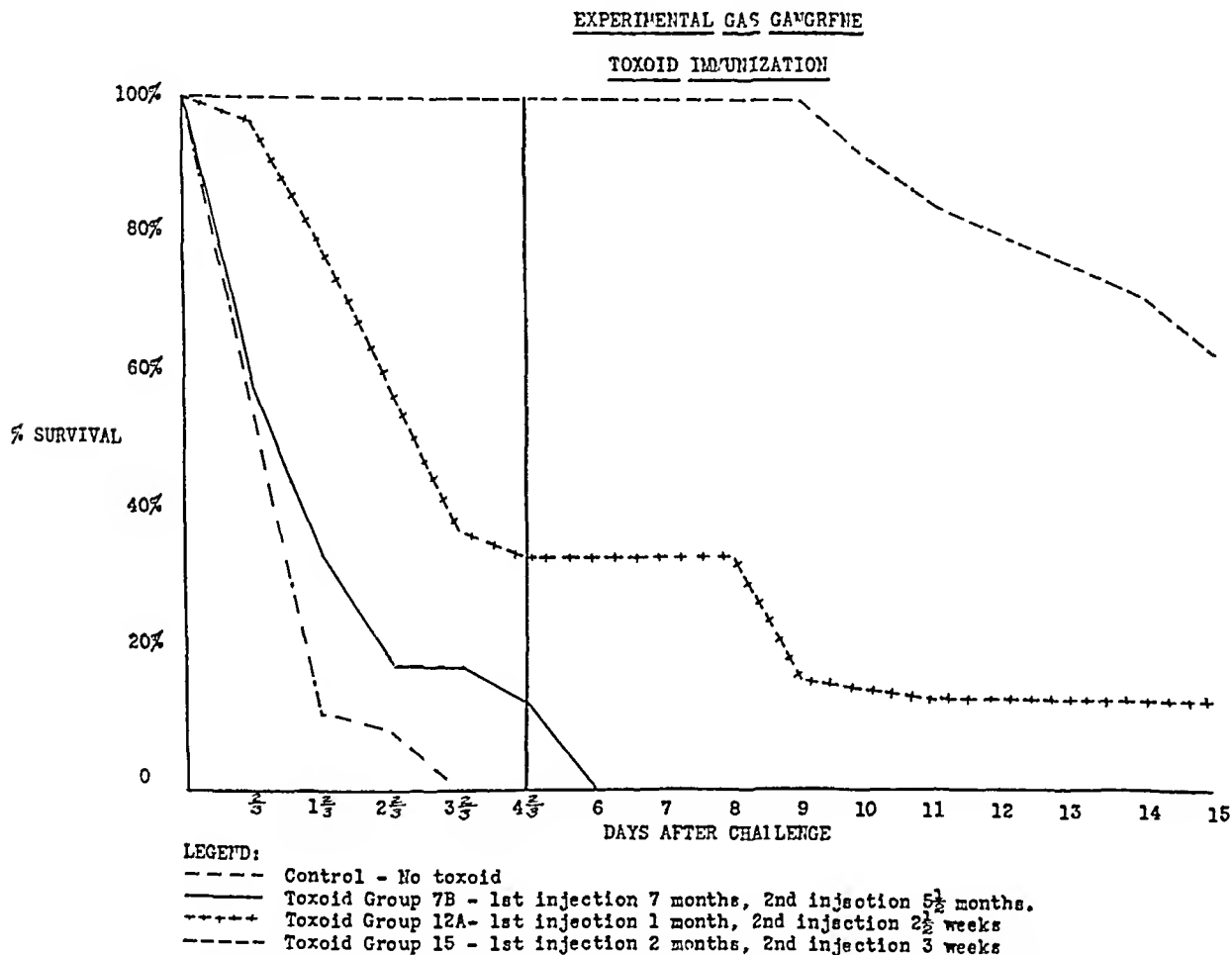


FIG 1—Comparing the degree of immunity produced by two injections of Cl welchii toxoid in doses of 30 Lbs over periods of one, two, and seven months. The results are depicted graphically as the rate and percentage of survival.

An increase in the number of injections to three, using the same dose of toxoid and over a period of two and 2½ months (Group 12B) produced a high degree of protection against challenge, 63 per cent of the animals surviving the 4½ day period (Fig 3). All of the control animals receiving one or more MLDs died in 3½ days of fulminating infections.

When the dose was increased to 40 Lbs and three injections were given at varying intervals (Group 16A, 16B, 16C, and 16D), different degrees of immunity were produced which varied with the time intervals between injection and challenge (Fig 4). The greatest degree of protection was found in



Group 16A in which the lesions were smaller and less severe and in which 95 per cent of the animals survived the  $4\frac{2}{3}$  day period when the injections were made  $5\frac{1}{2}$  months,  $4\frac{1}{2}$  months, and ten days before challenge

When each of two doses of toxoid was increased to 60 Lbs and given at

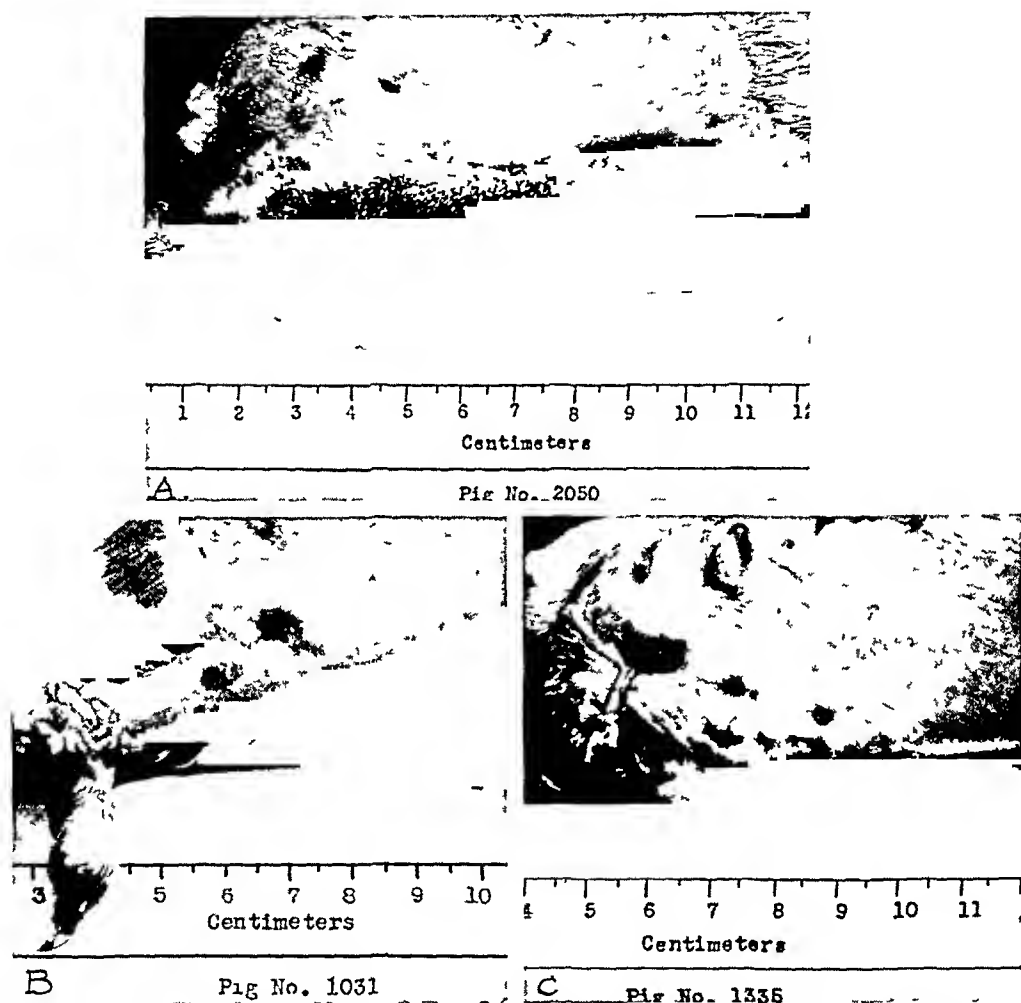


FIG 2—Comparing the appearance and extent of the lesions of gas gangrene produced by challenge with 1–10,000 MLDs of *Cl welchii* culture in representative animals of both control and toxoid immunized groups

A An example of the fulminating nature of this infection in an untreated or control animal 24 hours after challenge with 1 MLD of *Cl welchii* culture. Death occurred 40 hours after challenge. Note extension of process into abdominal and thoracic walls.

B Showing the very small and healing lesion of clostridial infection in a toxoid immunized animal 16 days after challenge with 100 MLDs.

C Illustrating the residual lesion of clostridial infection in a toxoid immunized animal that survived challenge with 10,000 MLDs.

one month intervals  $3\frac{1}{2}$  to four months before challenge (Groups 17B and 17D), and a third or booster dose of 30 Lbs was given 10 to 24 days before challenge, from 46 to 65 per cent of the animals survived the experimental infection produced by 1–100 MLDs of *Cl welchii*. In a third group (17A)

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similarly treated with toxoid but exposed to the overwhelming challenge of 100,000 MLDs only 23 per cent of the animals survived. The highest degree of protection was manifest in that group receiving the first injection  $3\frac{1}{2}$  months before challenge (Fig 5). All of the control animals receiving one or more MLDs were dead within  $2\frac{2}{3}$  days of a severe and extensive infection.

Because of the possibility of the toxemia of gas gangrene being produced in part by products arising from degenerating muscle, an attempt was made to measure any additional antigenic effect of injections of trypsin into muscle

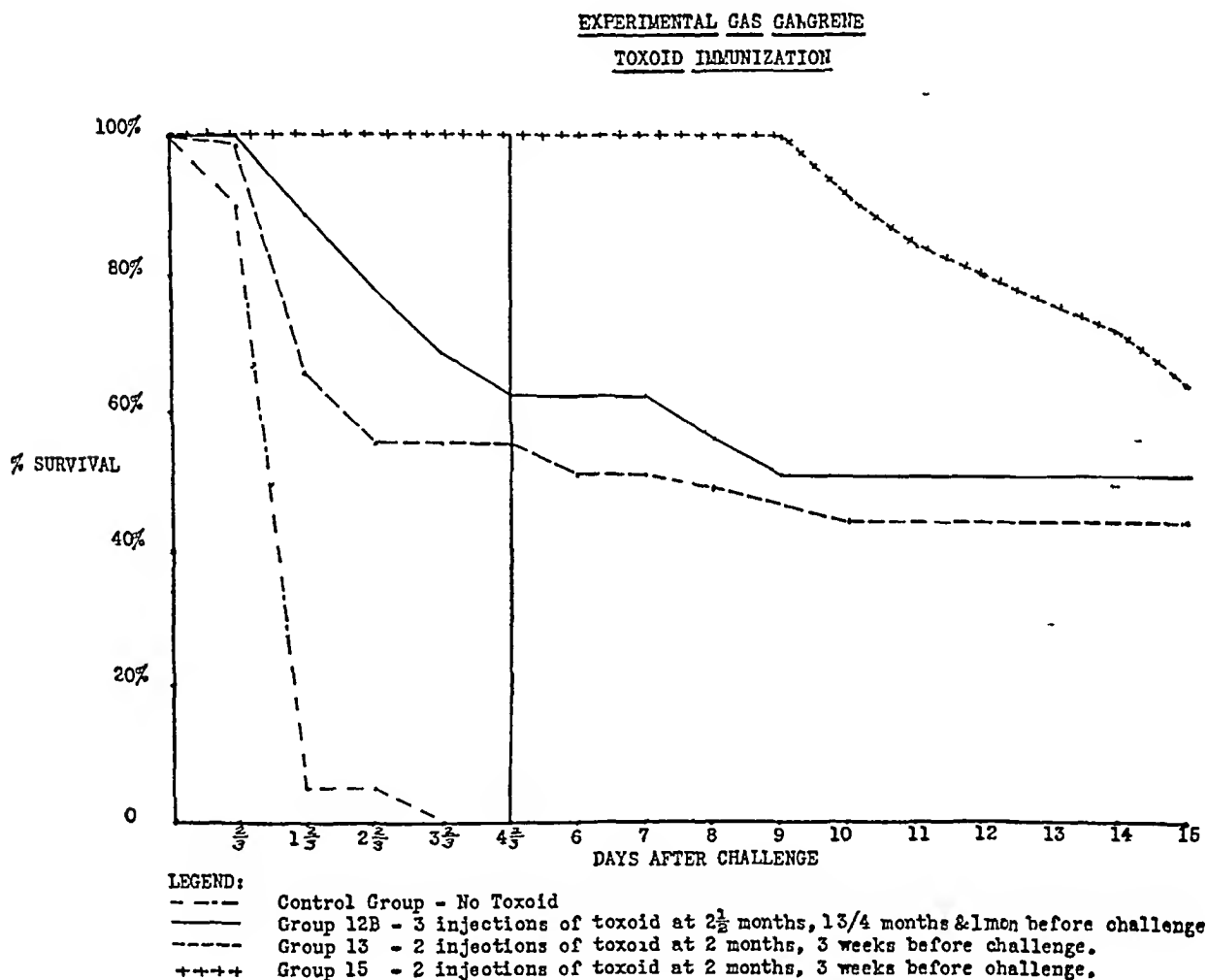


FIG 3—Comparing the degree of immunity obtained with three injections of toxoid over  $2-2\frac{1}{2}$  month period with that obtained with two injections over the same period using toxoid doses of 30 Lbs

along with toxoid. A group of 30 animals was subdivided into two groups of 15 animals each (Groups XVIIID and XVIIIDT). Both received three injections of 60, 60, and 30 Lb of toxoid at four months, three months, and 24 days respectively before challenge. In addition Group 17 DT received 12 daily injections of 8 mgms of purified trypsin. Challenge with 100 MLD's produced no significant difference in the rate of survival in the two groups (Fig 6).

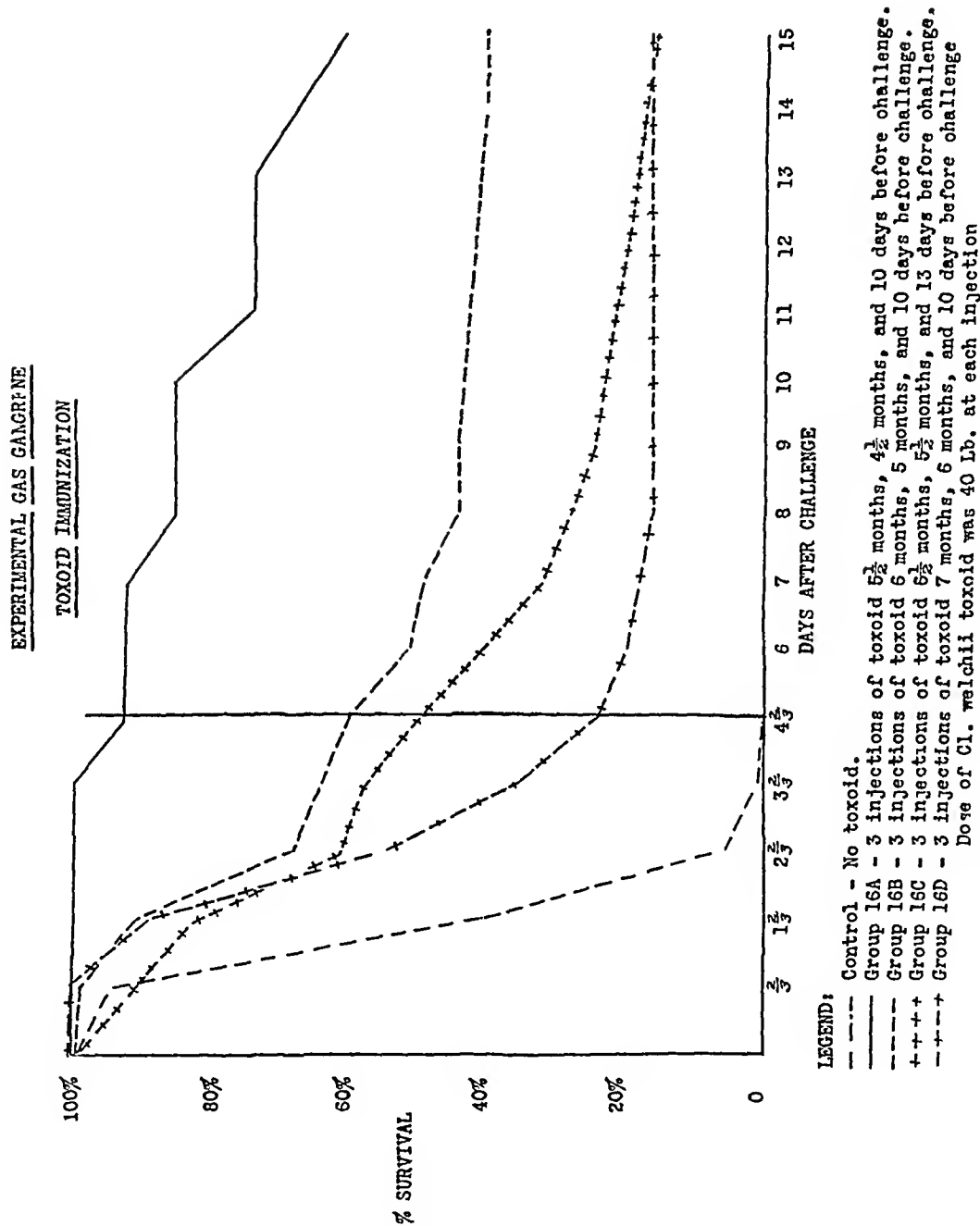


Fig 4—Illustrating the diminishing degree of protection produced by three injections of toxoid when the period of immunization was increased from 5½ months to seven months and the third or booster dose was given 10–13 days before challenge

Determinations of the serum titers of alpha antitoxin were made in 5-8 representative animals of the different groups. The levels varied considerably, ranging between 0.5 and 20 units per cc and averaging two and five units per cc. In Group 15, titers of 10 to 20 units were obtained and it was in this group that 100 per cent survival of the animals occurred during the test period of  $4\frac{2}{3}$  days. With this one exception there seemed to be no correlation between the alpha antitoxin level and the degree of protection in the animals previously treated with toxoid (Table II).

TABLE II

Type of Toxoid	Group	Number of Injections	Antitoxin Level (Units)	Percentage of Survival in 4-2/3 Days
H 21 A	7B	2	1-5	12
H 24	12A	2	2-10	33
H 24	15	2	10-20	100
H 24	12B	3	0.5-10	63
H 24	13	3	1-5	56
H 24	14A	2	5-10	70
H 25	16A	3	2-5	95
H 25	16B	3	2-5	60
H 25	16C	3	1-10 (2-5 Av.)	50
H 25	16D	3	1-2	24
H 25	17A	3	2-5	23
H 25	17B	3	1-2	65
H 25	17D	3	2-5	46
H 25	17DT	3	2-5	26
H 25	18A	2		28
H 25	19	2		52

#### ANALYSIS OF RESULTS

The problem of producing effective immunization with toxoid against gas gangrene is very complex. It is realized that *Cl welchii* is only one of many causative organisms in this disease but is the most frequent and probably the most important. Our investigations at this time have therefore been limited to its toxoid so as not to introduce other variables and unknown factors arising from the use of combinations with other toxoids. The problem of effective toxoid prophylaxis against experimental *Cl welchii* infections alone has been very complicated and difficult. In Table II it will be noted that three preparations of toxoid were used which were made identically in so far as is known from the same basic materials. However, somewhat higher degrees of protection were exhibited by animals injected with toxoid H 24 than those injected with toxoids H 21 A or H 25. In addition the highest alpha antitoxin titers were obtained with toxoid H 24. The significance of this observation has not been determined but it is known that different preparations of tetanus and diphtheria toxoid show varying degrees of antigenicity. Although the importance of certain factors has not been measured completely, it is evident that a high degree of immunity was produced in markedly susceptible animals against challenge with 1-10,000 MLDs of a highly virulent strain of *Cl welchii* in the presence of crushed muscle and dirt. According to available informa-

tion, no other type of toxoid has been subjected to such severe tests In addition it is questionable whether human beings are ever exposed to as many as 1,000 or 10,000 MLDs except under most unusual circumstances

Early in the investigation, only slight protection was obtained with 12 to 33 per cent of the animals surviving Subsequently the percentage of survival

EXPERIMENTAL GAS GANGRENE  
TOXOID IMMUNIZATION

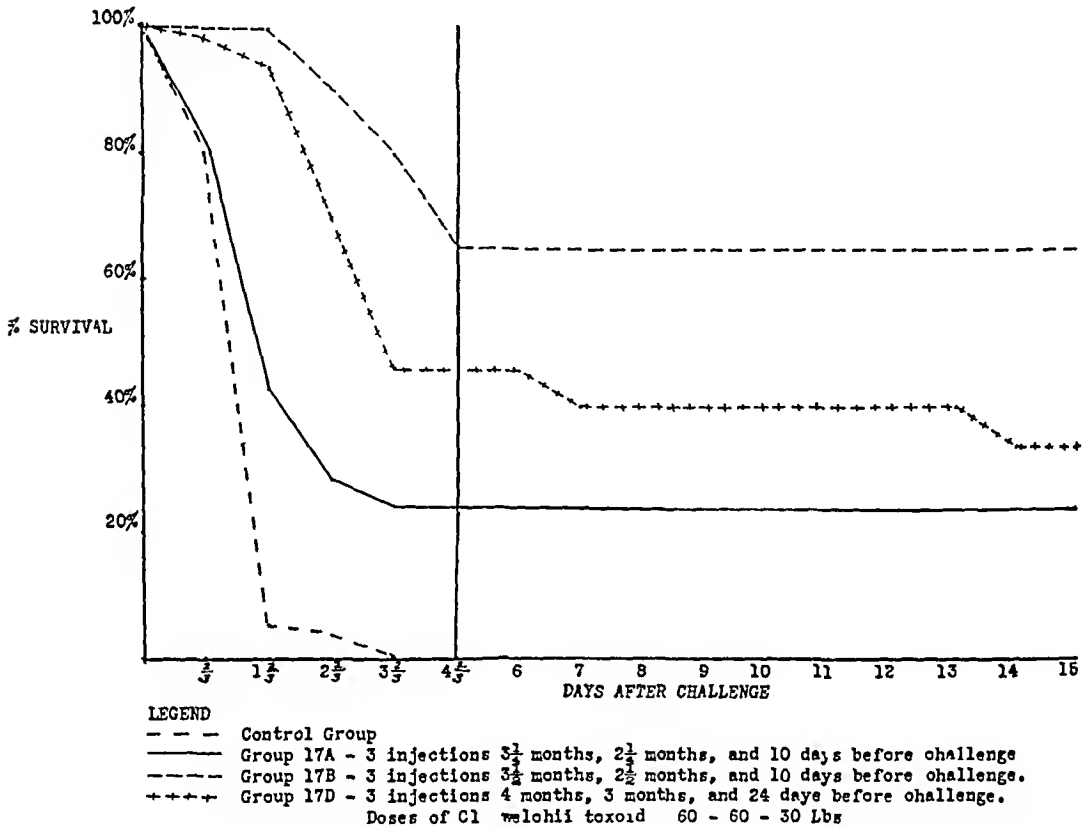


FIG 5—Showing the degree of immunity produced by three injections of toxoid during a period of  $3\frac{1}{4}$  to 4 months Group 17A received an overwhelming challenge of 100,000 MLDs

has been greatly increased, varying between 46 and 100 per cent under different conditions Because of the limitations of time, the duration and best methods of producing long term immunity have not been established as yet, and further work along this line is imperative

It is significant to note that serum antitoxin levels of one to ten units of alpha antitoxin have consistently failed to produce adequate protection against this type of infection, and only when the blood titers reached 10 to 20 units was 100 per cent protection obtained This is contrary to the belief that the presence of 0.1 to 0.25 units per cc of alpha antitoxin in the circulating blood is the critical level of immunity Thus the danger of measuring immunity in

EXPERIMENTAL GAS GANGRENE  
TOXOID IMMUNIZATION

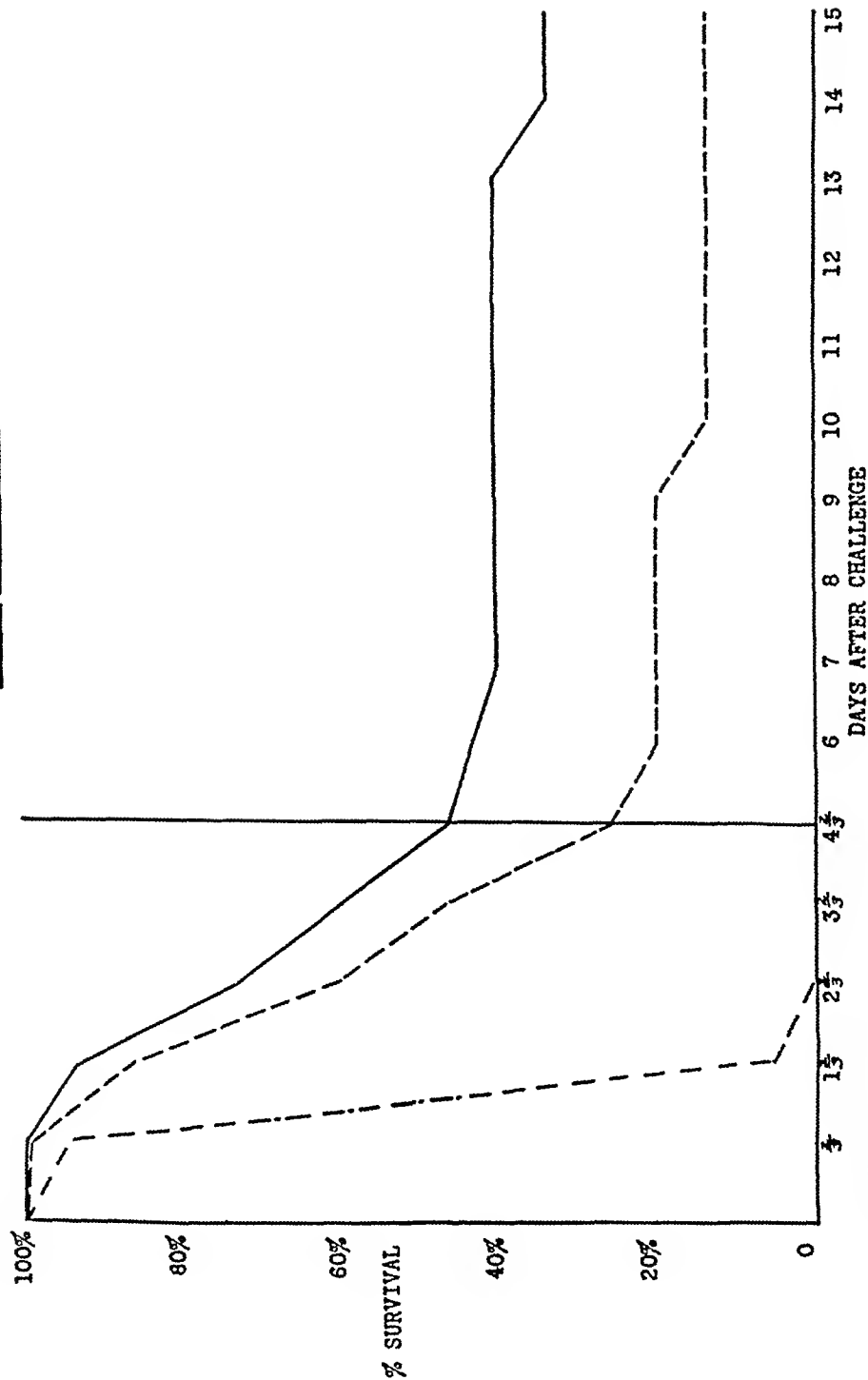


Fig 6 —Showing the lack of any additional antigenic effect of trypsin in toxoid treated animals

gas gangrene on the basis of blood antitoxin levels and the fallacy of assuming that levels of 0.1 unit per cc will protect human beings from actual infection is emphasized

In addition, the evidence indicates also that experimental gas gangrene produced in the presence of crushed muscle and dirt is more severe and definitely more refractive to toxoid prophylaxis than the type produced by the simple injection of bacteria, just as it was with chemotherapy.<sup>10</sup> The discrepancy between the high degree of protection (80 to 100 per cent) produced by toxoid injections in animals challenged by the simple injection of toxin or bacteria into healthy muscle and the much lower degree of protection in animals challenged by the injection of bacteria into operative areas containing crushed muscle and dirt suggests the presence of some factor or factors other than the known bacterial exotoxins contributing to the toxemia and mortality of gas gangrene. Our studies suggest that this other toxic factor is produced by the growth of virulent bacteria on the crushed muscle. The presence, nature, and methods of control of such factors are under investigation at the present time.

The production of a high degree of immunity against this severe form of *Cl welchii* infection in guinea pigs is significant, and it is an indication that effective and complete toxoid prophylaxis is possible in experimental animals, particularly if the nature and control of the other toxic factors can be worked out. Similar experimental studies with toxoids of the other clostridia associated with clinical gas gangrene have been started in anticipation of producing an effective mixed toxoid for ultimate clinical use.

#### SUMMARY AND CONCLUSIONS

The possibilities of producing effective toxoid immunity against a severe form of experimental gas gangrene developed in the presence of crushed muscle and dirt in animals whose susceptibility and antigenic response are similar to those of the human have been studied. Three hundred and sixty-four guinea pigs injected with *Cl welchii* toxoid at various intervals were challenged by this method. In the early experiments, the degree of protection was low, being 12 and 33 per cent, although blood antitoxin levels in excess of 0.1 unit per cc were produced before challenge. When similar groups of animals were challenged with injections of toxin or bacterial culture into healthy muscle, 80 to 100 per cent of the animals were protected by blood levels in excess of 0.1 units per cc. In subsequent experiments, however, modified procedures of immunization with toxoid have gradually increased the protection to 50 to 100 per cent of animals. The presence of an unknown factor or factors which contributed to the toxemia and mortality of experimental gas gangrene developing in the presence of crushed muscle and dirt is suggested by these studies. The high degree of immunity produced against the severe form of infection indicates that effective immunity is possible by the injection of toxoid against gas gangrene produced by *Cl welchii*, but the duration of the immunity is undetermined.

Other studies are in progress to increase and extend the degree of immunity afforded by injections of *Clostridium welchii* toxoid and to produce similar immunization with toxoids of the other clostridia associated with gas gangrene in anticipation of the development of an effective mixed toxoid for human prophylaxis against clinical gas gangrene

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DISCUSSION—DR JOHN S LOCKWOOD, New York I want to congratulate Doctor Altemeier with warm thanks for this splendid work The development of a toxoid against *Clostridium welchii* was one of the high priority projects of the Committee on Medical Research during the war It was the feeling of many of us that the methods of



testing employed by the chemists did not necessarily meet the severe conditions of the types of compound injuries in which gas gangrene so quickly develops. Doctor Altmeier has met this need with brilliant success and has proved that the toxoid against *Clostridium welchii* will meet experimental conditions of great severity. You are all familiar with the success of tetanus toxoid during the last war. It remains to be seen whether a similar measure of success can be achieved with toxoids against the organisms producing gas gangrene. I think we can question whether it will be possible in as short a time to develop as clearcut demonstration of the value of this toxoid as was the case with the toxoid against tetanus. But this large scale clinical experiment will probably have to be carried out some time. I am sure we will all await with interest the later stages of this important and promising study.

MAJOR GENERAL NORMAN T. KIRK, Washington. I want to congratulate Doctor Altmeier on this excellent research work in connection with the protection from gas gangrene diseases by the use of a toxoid. The development of a suitable toxoid for *Cl. welchii* infection had the highest priority so far as my office was concerned during the summer of 1943. A great deal of the work was done in the development of a toxoid by OSRD under the direction of the National Research Council. We were informed that the toxoid had been developed just about the time of V-E Day and that, so far as could be told from experiments with animals, it would give protection. It was our plan to immunize every other division invading Japan with this toxoid to test its worth in the human. Plans were under way to procure this toxoid from civilian sources when V-J Day came.

In World War I there were some 4000 major amputations. I should say that about 50 per cent of these amputations were necessitated to save life from gas gangrene. Fortunately our fears that the incidence of gas gangrene infection would be high in our Army in France did not materialize. There was a minimum of this disease in Italy, particularly in those troops whose evacuation from the site of injury to the forward surgical installations was delayed due to terrain difficulties.

The efficiency of tetanus toxoid was excellently demonstrated in World War II. There were only about eight cases in our Army. It is our hope that an equally effective toxoid can be developed for *Cl. welchii* and other organisms causing this disease before another world conflict. In total war, and with the atomic bomb, the civil population will need this protection as much as or more than the armed forces.

Again my congratulations and appreciation for this excellent bit of work that is being carried out at the University of Cincinnati.

DR. EDWARD D. CHURCHILL, Boston. I wish to emphasize the importance of this investigation not only to the military forces but to the civilian population as well. Doctor Glenn reported last year on the experience with tetanus in Manila. In the Army the incidence of gas gangrene can be reduced greatly by prompt evacuation and proper surgery, but in any disorganized situation, when there is a retreat, when transportation and medical facilities are completely paralyzed, the incidence of gas gangrene goes up immediately. In a disaster that involves the civilian population as war does today, gas gangrene will occur. So this project is one we hope will be continued with first priority.

DR. W. A. ALTEMEIER, Cincinnati (closing). I do not wish to imply that the excision of devitalized tissue in wounds is no longer necessary. This experiment was devised to test to the utmost the immunizing power of gas gangrene toxoid, but for obvious reasons surgical excision of devitalized tissue is just as important as ever. Apparently the antigenicity of preparations of toxoid made at different times has not been uniform, although every step in their manufacture seemed to be identical. Further experimentation is under way to produce toxoids with uniform antigenic activity. Finally, our goal is to develop a mixed toxoid which will be effective for all of the clostridia producing clinical gas gangrene.

I wish to thank all the discussors for their kind remarks.

# THE PATHOPHYSIOLOGY OF THE CAUSE OF DEATH FROM CORONARY THROMBOSIS\*

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TORONTO, CANADA

THE EXPLANATION OF THE CAUSE OF DEATH from coronary thrombosis by the cardiologist is frequently ventricular fibrillation or cardiac failure. The explanation of the reason for low blood pressure is very vague. Shock and reflex peripheral collapse are mentioned (Schwartz<sup>1</sup>). It seemed to me, that what appears to simulate a picture of shock with low blood pressure, as well as the fibrillation that frequently ensues, are inadequately explained by the theories in vogue at the present time. Measurements of circulation time, rate of blood flow, venous pressure, etc., have all added more information to the subject but have not demonstrated "why" there is a low blood pressure or "why" the heart fails either in fibrillation or without.

It is the purpose of this paper to discuss the results of some experiments that are very incomplete but which show to my mind the following points (1) Within a few minutes of tying a major branch of the coronary artery there is

- (a) Blueness over the area of distribution of the vessel
- (b) Dilatation of this segment of the heart muscle
- (c) Lack of contraction over this area
- (d) As soon as contraction of this area ceases there is paradoxical systole of the left ventricle. This probably is the most significant finding in relation to the signs under discussion
- (e) This is accompanied by an immediate fall in blood pressure
- (f) and a diminished left ventricular output

If these effects are allowed to continue there is fibrillation and death (2) If the ligature is released from the coronary artery before fibrillation sets in, then all these processes reverse themselves and everything returns to normal

## EXPERIMENTS

(a) The experiments are designed in the following way. With the pericardium open, a suture is placed through the apex of the left ventricle so that the heart is under control. A point on the anterior descending branch of the left coronary artery is selected, proximal to the two or three large terminal branches, over the middle portion of the left ventricle. This leaves one or two branches proximal to the site of ligature. The area of heart muscle supplied by these branches is outlined in one's eye and at roughly the periphery of these areas, two silk sutures are placed through the epicardium as markers, one placed toward the right and the other to the left of the area supplied by these branches (Fig 1)

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\* Read before the American Surgical Association, March 26, 1947, Hot Springs, Va



FIG 1—Showing the two markers placed astride large branches of the left anterior descending branch of the coronary artery. A loop of silk is placed loosely and not tied around the artery at the site at which it is to be tied.



FIG 2—Shows the similar area after tying the coronary artery. It shows the stretching of the area of the heart demonstrated with an increased distance between the markers. The vessels which are tortuous under ordinary conditions, here are stretched out and are taut.

(b) Measurements between these markers are made with callipers so that any change in size of this area of the heart can be measured. Next the coronary artery at the site selected above is exposed. The accompanying veins are protected and a silk ligature is placed around the artery at this point.

(c) The artery is tied and the time noted.

(d) Within a few seconds, measurements are continued to be made between the two markers on the surface of the left ventricle.

As well, a large branch of the aortic arch is dissected out, divided and a large bore cannula with a thickwalled rubber tube attached, is inserted and a bull dog clamp applied. The animal is injected with a large quantity of heparin. With this cannula in a large branch, the blood pressure of the aorta is measured on a manometer filled with saline and heparin solution. This rubber tube attached to the manometer is arranged so that it can be disconnected and the output from its end measured in a graduate.

It is noted within a very short time that there is an increasing distance between these two markers, indicating an expansion of the area of heart muscle supplied by the vessels which are now occluded (Fig. 2).

(e) Within one to one and a half minutes, the maximum expansion of this area of heart muscle is obtained and in all cases the expansion has been about 25 per cent above the measurements found, before the coronary artery was tied.

Before and after the ligature is tied on the coronary artery, the blood pressure is taken continuously on the manometer and the results have shown invariably that there has been a fall in blood pressure (Table I). This begins

TABLE I

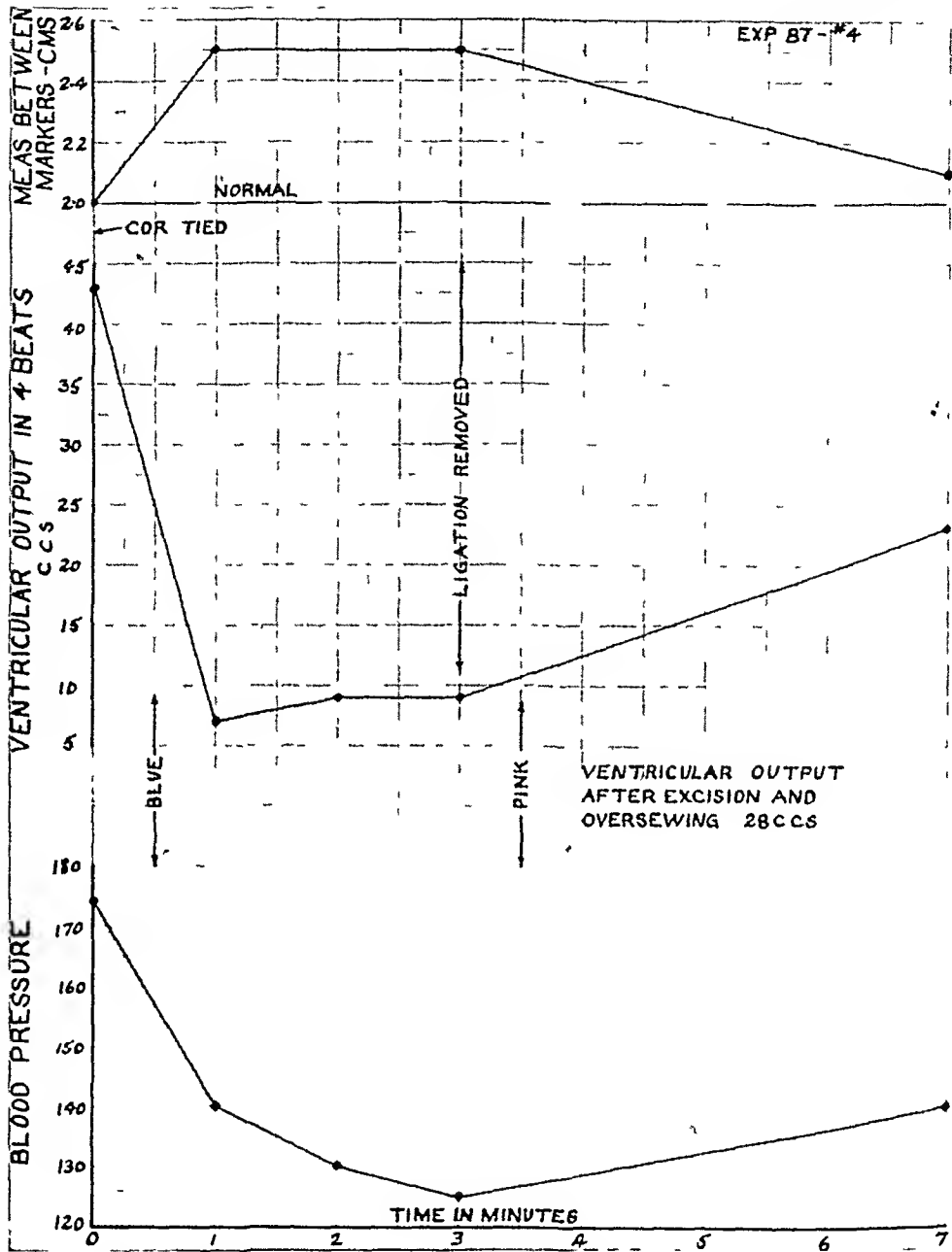
SHOWING THE TIME IN SECONDS FOR THE MAXIMAL INCREASE OF DISTANCE BETWEEN THE MARKERS

Exp. No.	Maximum Increase Between Markers		Time in Seconds	Exp. No.	Maximum Increase Between Markers		Time in Seconds
	Cms.				Cms.		
H1	0.5		60	H4	0.5		150
H2	0.65		120	H5	0.7		150
H3	0.6		180	H6	1.0		180

not immediately on tying the coronary artery, but becomes evident when there is obvious lack of contraction with stretching and dilatation of the area of the heart, which is about to become the infarct.

It is arranged at this stage that the cannula in the aortic branch is disconnected from the manometer, during some of the experiments, so that the output of the heart can be measured before and after (Graph I). This is done by allowing an open flow of blood through the large-lumen tube, directly into a graduate. The amount of output of the heart has fallen very considerably on all occasions (Graph II).

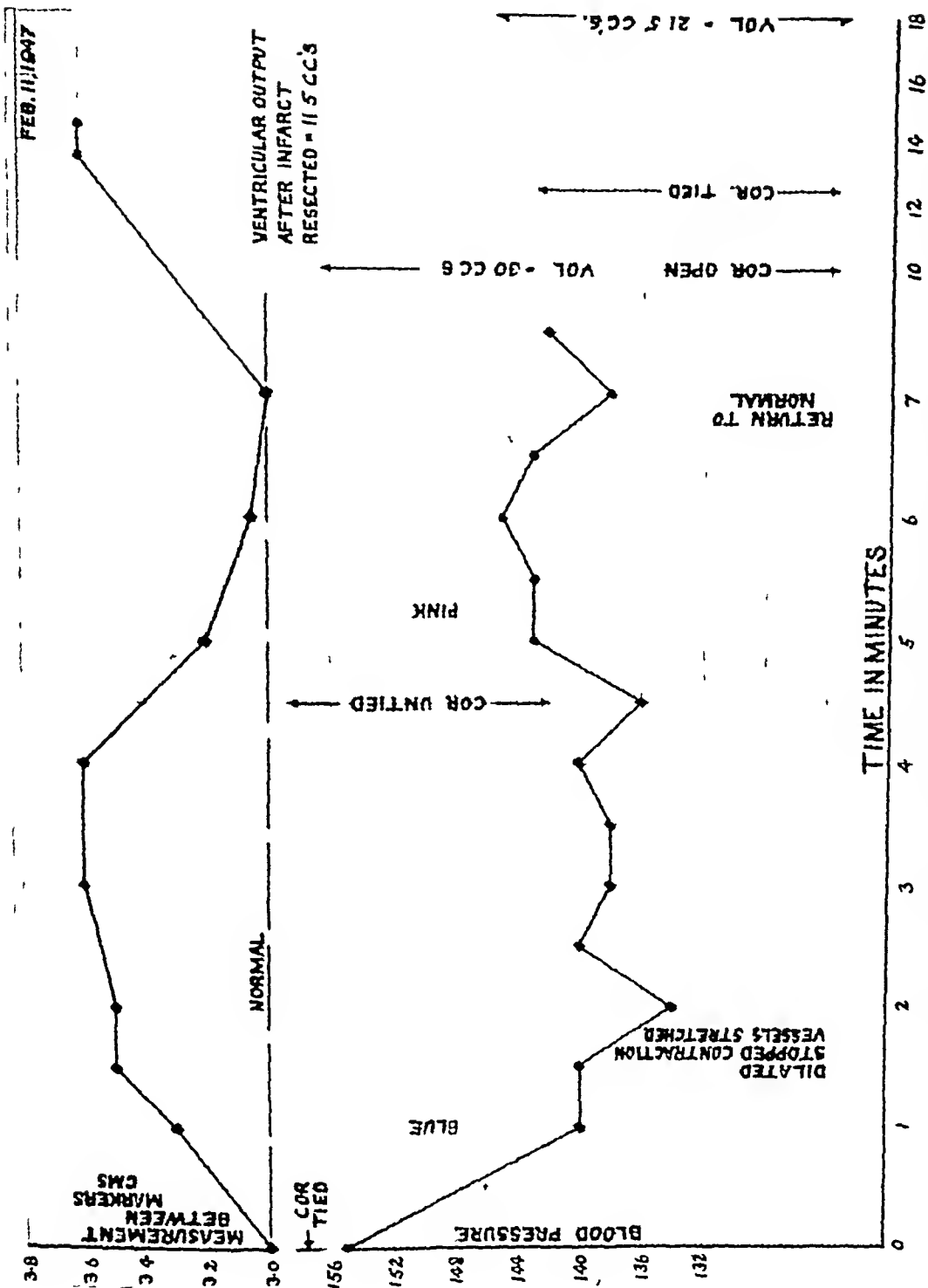
The cardiac output experiment is done frequently with the aorta unclamped and in other cases it is done with the aorta clamped off distal to the branch being used, so that most of the ventricular output appears through the open cannula. After withdrawing the blood, which is measured for five beats



GRAPH I—Graph showing the effect produced following ligation of the coronary artery. There is

- (1) An increased distance between the markers as shown in the measurements in the upper line
- (2) The next line shows the blood pressure fall

When the tie is removed from the coronary artery within two to three minutes the infarcted area regains its color. Its expansion shrinks down to normal again. The vessels again become tortuous. The blood pressure and cardiac output return to normal and the distance between the markers returns to normal. If, however, the tie is left on too long, the condition becomes irreversible. Then the infarct remains as a permanent effect and within a very few minutes the animal will die. With an infarct which does not recover, the animal is losing his blood pressure and cardiac output, there is visible dilatation of the right heart until this becomes enormous. In other words, the left ventricle is unable to put out the amount of blood which is returned to it and this goes through a progressive change until with failure of the left ventricle, the right ventricle is dilated enormously and ultimately fails with fibrillation of both left and right ventricles.



GRAPH II—Showing increased distance between markers and fall in blood pressure with diminished output with coronary tied, then untied and finally tied again

on each occasion, the blood is returned to the animal so that the blood volume is not changed throughout the remainder of the experiment

Electrocardiographic tracings are also made during the different stages of doing this experiment so that the effect here can be compared with those which can be demonstrated by the other methods of investigation

To prevent the expansion of the infarcted area a patch of firm cloth is stitched to the epicardium around the periphery of the area to become infarcted, before the artery is tied off. This is stitched down in such a way that the cloth is taut and will tend to prevent bulging when the infarct begins to make its appearance. Under these conditions there is a drop, but less of a drop of blood pressure and not so great a fall in the cardiac output

#### RESECTION OF VENTRICLE

The next part of the experiment has to do with an attempt at overcoming the effect of such a coronary occlusion. When the artery has been tied off and

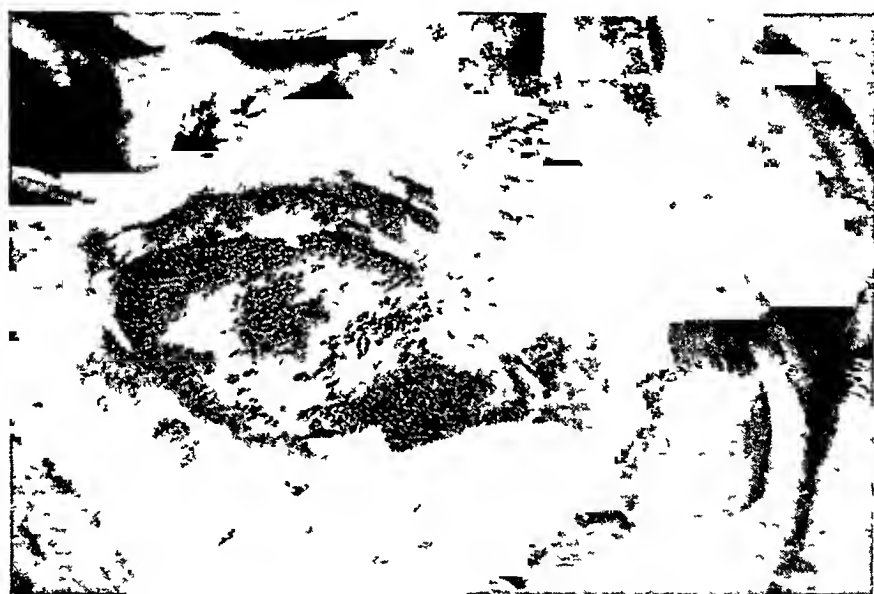


FIG 3—Shows the infarct resected and still holding by a pedicle which will be removed. The sutures are in place.

there is maximal dilatation of the area to be infarcted, with the fall in blood pressure, and the diminished cardiac output, then an attempt is made to resect the infarcted area of the left ventricle (Fig 3). This has been accomplished quite satisfactorily in 25 dogs and has been done in the following way:

The area infarcted is easily visible. A continuous mattress-type of cat-gut suture is passed through the ventricle approximating the margins of the infarcted area, leaving the infarcted area projecting out of the cardiac cavity as a loop. When this has been tightened up, fairly satisfactory hemostasis is obtained. The infarcted area can then be excised quite neatly with a scalpel, taking care not to cut the suture which is vital at this time. Following re-

removal of the infarct, the area is again oversewn and a satisfactory repair can be obtained. In some the total repair has been done with cat gut, in others silk sutures have been applied on the surface to add more support.

The results of removing this infarct produce an astonishing effect in the animal. The cardiac output increases considerably and the blood pressure rises moderately although it does not return to the original level. When this has been done satisfactorily, the animal which one would judge, from control experiments, would die, survives quite satisfactorily and most of them have made quite a good recovery. In my experience, I would think that practically all animals in whom we had resected this area would have died of dilatation and finally fibrillation and heart failure. It is interesting, therefore, that many of these animals are alive and quite well for as long as one to two years later.

The accompanying photographs show the cross sections of hearts of animals which were sacrificed at the times given and show the state of the wall of the ventricle after resection of the infarct (Figs 5, 6 and 7) at the various intervals. These animals following resection of the ventricle are not in bad health but recover very quickly and within a short time carry on as do normal animals. There seems to be no limitation of function and no disability on this account. They are quite vigorous and strong and have plenty of energy.

#### DISCUSSION

My thoughts and experiments on this subject lead me to believe that when a coronary attack occurs, whether it be spasm or complete occlusion, an infarct is produced in the heart muscle. If it is placed so that it involves the conducting mechanism, it may interfere with conduction and embarrass the heart, from that point of view. If the conducting mechanism is not involved, then it produces an area, which within a very short time is non-contractile. This area becomes dilated and acts as an expansion chamber. When the ventricle contracts, varying amounts of the blood of the ventricle, depending on the size of the infarct, are forced into this elastic chamber. The effectiveness of the contraction is partly lost because of this expanding chamber and consequently the amount of blood delivered into the aorta is much diminished. This paradoxical systole (Fig 8), to my mind, probably accounts for many of the symptoms from which the coronary patient suffers, namely low blood pressure, signs of shock, lack of energy, and all the symptoms related to this lack of adequate peripheral circulation. It provides an explanation for the picture of shock which is evident in many of these patients. If the condition persists or the infarct is of a fairly large size, depending on the reserve power of the remainder of the heart, the patient goes through progressive changes until ultimately fibrillation or failure occurs, but these are terminal events only.

The medical treatment of such a condition can be palliative only. Measures to try to increase the blood pressure and blood volume may improve the situation somewhat, but there is nothing that can be done to this expansion chamber, produced by the infarcted area, to make it function better. There



are no drugs that have any effect on this. They may whip up the remaining heart muscles to make a greater effort, but much of this effort is lost in the expansion chamber. This is a situation somewhat similar to the state of affairs in an arteriovenous aneurysm or peripheral aneurysm elsewhere. In a clinical patient it is possible that the degree of fall of blood pressure, is a measure of the size and significance of the expansion chamber, produced by the infarcted area. This is fairly well born out by the fact, that clinicians are quite aware, that the patient who has a very low blood pressure, is the patient who is in the more critical condition, as a result of his coronary occlusion.

#### TREATMENT

While it is obviously facetious at this stage to make the following remarks, still I have a conviction that, as medical treatment is so ineffective, and is entirely helpless, except from a palliative point of view, the day may come, when the best plan of dealing with a coronary thrombosis, would be an emergency operation. This should be undertaken before the patient gets a large expansion chamber, which will ultimately cause heart failure. The approach is not difficult, and the right or left coronary areas could easily be excised and repaired with relative safety. This would accomplish two things. (1) It would overcome the immediate effect of the expansion chamber and save the patient from cardiac collapse. (2) As well it would remove the infarcted area, so that the coronary artery, which was occluded, would from then on, be of no significance. It would as well, remove the part of the heart in which a cardiac aneurysm may develop and which ultimately may rupture. As well it would relieve the patient of the dangers of acute rupture of an infarct, within a few days of the time of infarction.

This perspective, then places on the cardiologist the responsibility of being able to decide, just where in the heart, is this infarcted area. If it involves the anterior descending branch of the left coronary, which is the commonest site, this is readily accessible, and is quite easily dealt with surgically. If it involves the posterior surface of the left ventricle, or the left lateral surface, this also is easily dealt with. The area so far, which is relatively inaccessible, is the septal area but with an infarct involving the septum, if it does not interfere with the conducting mechanism, it is supported somewhat, by pressure of the right ventricle, and so far as I can see from recorded writings,<sup>2</sup> is less likely to produce aneurysms, ruptures and the other acute catastrophes.

As this is making drastic inroads on the physician's territory, I have some doubts if my colleagues in medicine, will consider, that surgical treatment of this lesion is reasonable. Possibly I may not see a suitable case on which this could be done, but I feel at the present time, that in a properly selected case, this could be done with dispatch, with less danger than waiting for the unpredictable effects of the coronary occlusion to develop, and that ultimately the patient might be cured.

The question of the anesthetic is not a serious one, because there is some evidence to suggest that a patient under ether anesthesia is in less danger

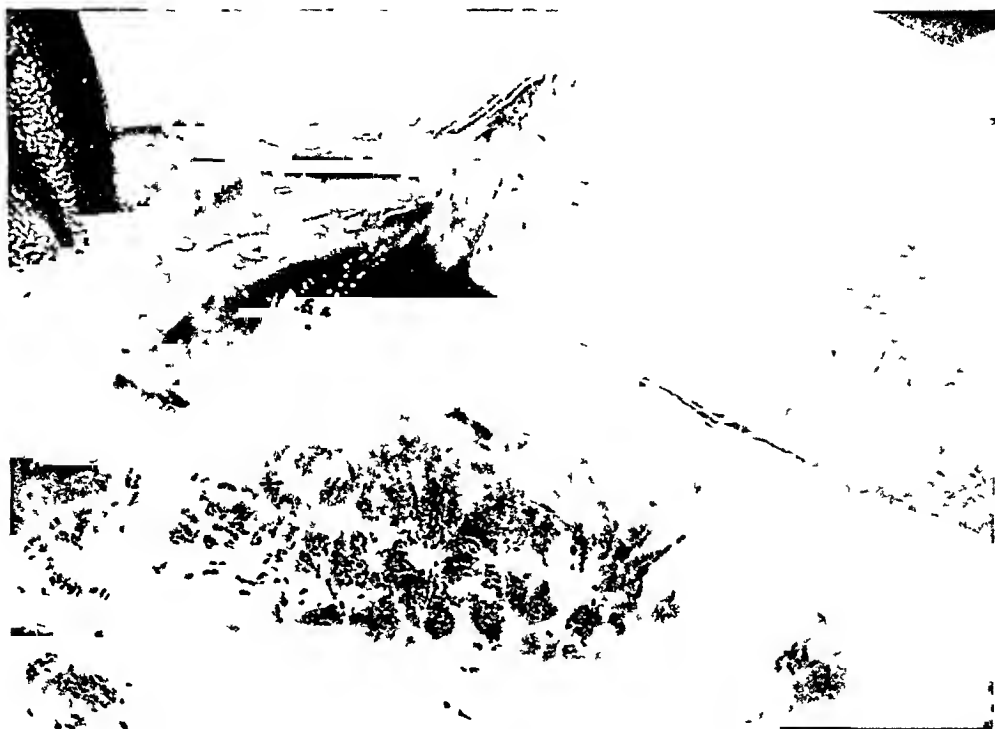


FIG 4—Shows the infarcted area removed and the defect repaired by sutures giving satisfactory hemastasis



FIG 5—Photograph of a cross section of the left and right ventricles showing the site of resection of an infarct one year previously. There is scar uniting the muscle on each side. There is a good lumen to the left ventricle and the remaining muscle is normal.



FIG 6—Low power of scar at site of resection of infarct of left ventricle



FIG 7—Photomicrograph showing the appearance of the scar uniting the left ventricle at the site at which the infarct was excised

with a coronary occlusion, than he is without the anesthetic. It might be a valuable measure to apply, for its immediate effect, and if the infarcted area were resected the patient might waken up with better prospects of survival, and of cure of his disease, from this particular attack.

#### SUMMARY

(1) A condition of paradoxical systole has been demonstrated experimentally in hearts in animals following coronary occlusion.

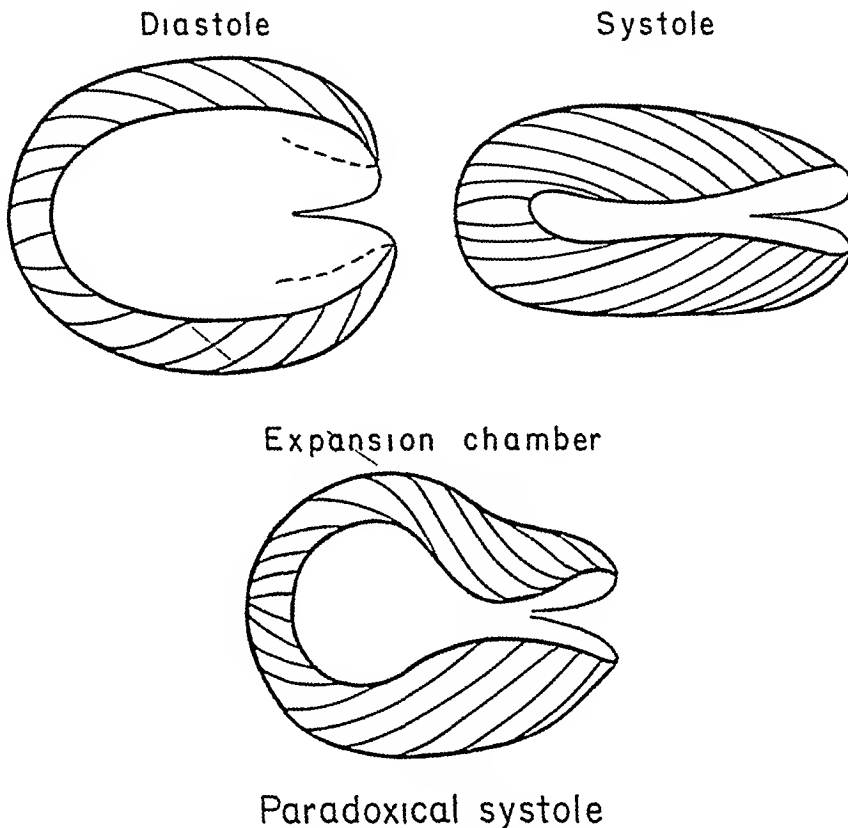


FIG 8—Diagrammatic representation of a ventricle in full dilatation, then the relative occlusion of the cavity with systole, and next the diagrammatic representation of the expansion chamber produced by the infarcted area which makes it impossible for the ventricle to empty itself or to deliver its regulation amount of blood, both because of the expansion chamber and secondly because there is less muscle area in its wall with the ability of contraction to expel the normal contents.

(2) This state is accompanied by a fall in blood pressure and diminished cardiac output.

(3) Following resection of the infarcted area in the heart, there is an improvement in blood pressure and in cardiac output.

(4) It has been demonstrated that compared with a control group of animals, the prospects of survival are 80%.

(5) It was suggested that the best treatment of acute coronary occlusion in the human being in selected cases might be, by immediate surgical operation. This would provide

- (a) A better chance of survival from the effects of a severe and large infarct from a major occlusion and
- (b) A cure of the patient from an infarcted area of the heart which would eliminate the dangers of acute rupture, aneurysm and subsequent rupture It would remove all the effects of a coronary occlusion

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1939

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I acknowledge with pleasure the technical assistance of Mr Newell Thomas and Dr E Delorme employed by the author, and Dr Ray Heimbecker for his photography This work was done without University or other assistance, apart from limited laboratory facilities in the Banting Institute

DISCUSSION—DR ALFRED BLALOCK, Baltimore I was sitting next to Dr Rudolph Matas while Dr Gordon Murray was presenting his paper and he stated to me that this work may be epoch-making The lack of prolonged discussion is probably due to the fact that others are as amazed by these brilliant experimental observations as I am

There is no more important problem in medicine and surgery than that which Doctor Murray is tackling Coronary occlusion ranks high in the list of causes of death A great deal of work is being done in various laboratories in an effort to find a satisfactory treatment for this common disorder Fortunately more money will be available in the future for additional studies on heart disease

It is only natural that Doctor Murray would hesitate to transfer immediately his experimental observations to the treatment of the patient When one realizes that the average survival period of patients who survive the first attack of coronary occlusion is approximately five years, one hesitates to carry out what appears to be at this time a radical surgical procedure I doubt if such a procedure appears to us to be more radical and bold than did the suture of heart wounds 50 years ago

The fact that Doctor Murray was able to prevent the death of animals following coronary occlusion by excision of the infarcted area is a magnificent accomplishment I believe that there will ultimately be a clinical application for his findings and it is to be hoped that Doctor Murray will continue and extend his studies

# FACTORS LIMITING SURGERY FOR ESSENTIAL HYPERTENSION\*

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## INTRODUCTION

THE SURGICAL TREATMENT of essential hypertension has been based on the concept that it is due to overaction of the sympathetic nervous system. Such overactivity has been attributed either to a disturbance in the higher functions of the brain, or to a decrease in the inhibitory influence of the moderator afferent nerves from the carotid sinus and the arch of the aorta. The increased activity of the sympathetic nervous system has been pictured as causing general or local vasoconstriction and an increased secretion of epinephrine. More recently such overaction has been regarded as responsible for the constriction of the renal blood vessels, thus leading to a release of renin.

To counteract the effect of sympathetic overaction and to lower the blood pressure, it has been deemed advisable to enlarge the vascular bed by denervation. In addition, the operations also denervated the adrenal medulla and the kidney blood vessels.

It is the purpose of this paper to present evidence that the entire concept of overactivity of the sympathetic nervous system as an important and primary cause of essential hypertension should be abandoned. It is also hoped that the presentation of a new concept of the pathogenesis of essential hypertension will indicate how operations on the sympathetic nervous system can modify the initiating factors of essential hypertension. Knowing these facts, it will be possible to outline the limits beyond which some operations as now practised are useless and may be harmful.

## EFFECTS OF OVERACTION OF SYMPATHETIC NERVOUS SYSTEM

Through experimental and clinical observation the manifestations of overaction of the sympathetic system are well known. Among those easily recognized are dilation of the pupil, pallor of the skin, increased activity of the sweat glands, tachycardia, salivation, hypertension of the diastolic type and hyperglycemia. Restlessness and tremor are characteristically present, an indirect effect of epinephrine release. Similar signs and symptoms are exhibited in persons in whom tumors of the adrenal medulla cause diastolic hypertension. It is accepted that the excess release of epinephrine has effects similar to overaction of the adrenergic fibers of the sympathetic nervous

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† Recipient of a grant in-aid-of research from the Commonwealth Fund.

system. However, in persons with essential hypertension such evidence of overaction of the sympathetic nervous system is not seen. They are exhibited to a marked degree in children with acrodynia, where diastolic hypertension is a constant finding.

#### THE CIRCULATION IN ESSENTIAL HYPERTENSION

Studies of the circulation in essential hypertension have shown that the raised arterial pressure is not due to an increased cardiac output or to increased blood viscosity, for these have been measured and found normal. It is recognized that diastolic hypertension is due to narrowing of the small arteries and arterioles. The hydrostatic pressure within the capillaries, the venules and the veins is normal. Intensive studies of the conditions of blood flow through the various tissues of the body such as the skin, the muscles, the brain and the kidneys in essential hypertension have been carried out (Pickering, 1935). It has been found, for instance, that the arterioles of the skin are narrowed, but that when the vasomotor influences are removed reflexly or by chemical block, the increase in blood flow is no greater, but sometimes a little less in subjects with benign and malignant hypertension than it is in subjects of comparable age with normal pressures. On such evidence it has been concluded that in essential hypertension the hand vessels are narrowed by a non-nervous agent, and this narrowing is of an order which, if generally distributed throughout the body, would account for the hypertension. Since the skin vessels are rarely and inconsiderably involved in the arteriosclerosis of hypertension, the narrowing is presumably not of structural but of humoral origin. Goldring, Chassis, Ranges and Smith (1941) have investigated, through the use of diodrast and inulin clearances, the renal circulation in 60 cases of essential hypertension of all grades of severity, and found that the effective renal blood flow as inferred from the diodrast clearances was reduced, the rate of the glomerular filtration is much less reduced than the tubular function so that the fraction of the renal blood flow filtered off into the glomeruli is increased. They also found that in all but three cases the renal excretory mass was reduced. It was evident from their studies that in hypertension, including essential hypertension, the efferent glomerular arteries are constricted. These investigators concluded likewise that in essential hypertension the vasoconstriction in the renal arterioles is not nervous in origin because the renal blood flow is not increased, nor is the filtration fraction lowered by operations in which the sympathetic nerve supply to the kidneys has been divided.

The second hypothesis that essential hypertension could result from overaction of the sympathetic nervous system because of underaction of inhibitory influences normally arising in the carotid sinus and the aortic arch, received support when it was shown by Koch, Mies and Nordmann (1927) among others that section of the carotid sinus and the depressor nerves could produce hypertension. However, it was shown by Pickering, Kissin, and Rothchild (1936) that the carotid sinus mechanism is active in essential hypertension.

and the tachycardia, which is a constant feature of this type of experimental hypertension, is not present in humans with essential hypertension

Evidence that in essential hypertension the vascular narrowing is humoral and not primarily nervous, is found also in the observation that during surgical anesthesia with ether when the skin is pink, indicating vasodilation, the blood pressure remains well elevated above the levels observed in persons with normal blood pressure under similar conditions. The persistent elevation of the blood pressure cannot be attributed always to generalized occlusive changes because the blood vessels as seen in muscle and renal biopsy material may show minimal degrees of occlusive narrowing (Castleman and Smithwick, 1943)

#### THE PATHOGENESIS OF DIASTOLIC HYPERTENSION

The results of studies of Cushing's syndrome have been utilized as a basis for a concept of the pathogenesis of essential hypertension because in both states there invariably develops diastolic hypertension and arteriolar sclerosis. Studies of the circulation in Cushing's syndrome have demonstrated that it is similar in its essential characteristics to that exhibited by persons with essential hypertension. Thus, the skin vessels in each are constricted but the degree of constriction is such that the blood flow through them under the existing increased arterial pressure is normal or only slightly reduced. In both the efferent glomerular arterioles are constricted first, and then with progression of the disease processes the total renal blood flow also is reduced.

The primary causes of Cushing's syndrome have been shown to be a tumor of the adrenal cortex, a tumor of the thymus, a tumor of the ovary, or an atrophy of the hypothalamic nuclei, particularly the paraventricular and the supraoptic (Heinbecker, 1946). These are the nuclei which innervate the neural hypophysis and control its function. It has been established that most, if not all, persons with Cushing's syndrome, regardless of the primary cause, exhibit some degree of polyuria and of polyphagia. It has also been established that regardless of the primary cause, there occurs a degeneration or hyalinization of the basophil cells, while the eosinophil cells are relatively or actually increased in number. Evidence of overaction of these eosinophil cells is indicated by a decreased insulin sensitivity, by a decrease in the lymphocytes of the circulating blood, by masculinization, and by the development of obesity. Evidence for these statements is based on the results of experimental studies previously reported on (Heinbecker, 1944), or now in process in our laboratory. For dogs, it has been concluded that the eosinophil cells are trophic to the adrenal cortex. This harmonizes with the observation of functional overaction or of hypertrophy so frequently encountered in persons with Cushing's syndrome when no actual tumor of the adrenal cortex is present. The hyalinization or degranulation of the basophil cells is considered to be associated with underaction, because of the elevated blood cholesterol and the diminution in basal metabolic rate observed in such persons. Experimentally it has been shown that the basophil cells are trophic to the thyroid gland and to the germ cells.



An experimental basis for the preponderance of the eosinophil cells with a depression of the basophil cells has been obtained in experimental studies in the dog (Heinbecker, White and Rolf, 1944). It has been established that when the neural hypophysis is denervated a marked cytological change occurs in the glandular hypophysis. Basophil cells disappear, while the eosinophil cells are preponderant and apparently overactive. The interpretation is made that through loss of the secretion of the neural hypophysis, or its neutralization when a tumor of the adrenal is the primary cause, maturation of the basophil cells fails to occur, while the eosinophil cells mature and are stimulated. A similar but less marked preponderance and overaction of the eosinophil cells follows a lesion in the posterior hypothalamus severing the fibers between the thalamus and subthalamus and the paired paraventricular nucleus. It also follows a production of partial asphyxia of one adrenal and the wrapping of one kidney in silk with removal of the other. It is significant that these experimental procedures give rise to varying degrees of diastolic hypertension. There develops in pregnancy also a preponderance of eosinophil cells in the glandular hypophysis. It is presumably due to overaction of these cells that there develops an enlargement of the adrenal glands. In those constitutionally susceptible, pregnancy may be associated with the development of diastolic hypertension.

Evidence from experiments on dogs, which will be presented in detail elsewhere, is believed to afford an explanation of the manner of development of diastolic hypertension in these various states. It has been found that following the administration of an extract from the anterior lobe of the pituitary or of adrenal cortical extract or, and particularly, by the simultaneous administration of these two extracts there results a constriction of the efferent glomerular arteries (Heinbecker, Rolf and White, 1943, White, Heinbecker and Rolf, 1947, in press). This in turn, by decreasing the blood flow to the renal tubules, is considered to lead to a release of renin. The combined action of these three humors is held responsible for the extra-renal arteriolar narrowing and thus for the development of diastolic hypertension.

To account for the development of hypertension in persons where there are no recognizable primary causes such as have been demonstrated in Cushing's syndrome, and who therefore have been designated as having essential hypertension, it is postulated that functional influences in the central nervous system, particularly in the frontal lobes of the cerebral cortex, normally may depress the hypothalamic nuclei which control the secretion of the neural hypophysis. The anatomic and physiologic bases for such influences are well established. On depression of the functional activity of these nuclei there results a diminution in the secretion of the neural hypophysis. This, on the basis of the experimental evidence presented, can be assumed to result in a stimulation of the eosinophil cells of the glandular hypophysis and these in turn to stimulate the adrenal cortex to greater activity. The combined influence of the anterior pituitary hormone and of the adrenal cortical hormone is to effect a constriction of the efferent glomerular arterioles of the kidney and

a release of renin. The combined action of all three humors here as in Cushing's syndrome is held responsible for the arteriolar narrowing and the development of diastolic hypertension.

It is apparent that according to this hypothesis all persons with diabetes insipidus might be expected to develop essential hypertension. Analysis of recent cases at Barnes Hospital has revealed that four of 12 persons with persistent marked diabetes insipidus, indicating thereby the presence of some glandular hypophysis (Heinbecker, White and Rolf, 1947) exhibited a diastolic blood pressure above 100 mm Hg. While this percentage incidence is higher than that which occurs in the normal population it indicates nevertheless that in order to account for the development of essential hypertension in persons who do not exhibit diabetes insipidus, it is necessary to postulate that not only must there result a sufficient functional depression of the neural hypophysis as a result of influences within the nervous system, particularly from the frontal cortex, but there must be also a susceptibility of the smooth muscle of the blood vessels to the vasoconstricting action of the humoral agents involved in the production of diastolic hypertension.

Other experimental evidence indicates that the combined overaction of the eosinophil cells and the adrenal cortical hormone increases the deposition of neutral fats in certain tissues, including the blood vessels, and raises the cholesterol content of the plasma (Heinbecker, White and Rolf, 1944, loc cit). Evidence indicating that such metabolic disturbances are of primary importance in the development of arteriolar sclerosis in persons with Cushing's syndrome has been presented (Heinbecker, 1944, loc cit). It seems reasonable to assume that they play a similar role in the development of the arteriolar sclerosis when associated with essential hypertension. Thus, the same influences which lead to hypertension are regarded as leading to the arteriolar changes associated with it.

#### DISCUSSION

If one accepts the implications of the studies of the circulation in diastolic hypertension, it is clear that such hypertension can no longer be attributed mainly to overaction of the vasomotor nervous system. Likewise, an analysis of the clinical signs and symptoms exhibited by persons with essential hypertension lends no support to the idea. In contrast, the clinical signs and symptoms associated with the diastolic hypertension in persons with acrodynia and in the hypertension associated with epinephrine secreting tumors, the pheochromocytomata, are easily recognizable and in clear agreement with the responses of stimulation of sympathetic nerve trunks or of the intravenous injection of epinephrine in man and the experimental animal.

The concept of the pathogenesis of diastolic hypertension herein presented affords an explanation for many difficulties associated with the acceptance of others previously presented. First, it offers a reasonable explanation as to how functional disturbances in the central nervous system can modify the function of the glandular hypophysis and thereby of all endocrine glands.

normally under its trophic influence without the existence of any direct nervous connection between the neural and the glandular hypophysis. It also provides a mechanism for the constriction of the efferent glomerular arterioles of the kidney, and thereby for the release of renin other than overaction of the sympathetic nervous system. Clinical studies of hypertension have shown that the latter hypothesis is not tenable. The concept presented here provides for an initiating humoral mechanism for the activation of a renin mechanism not of primary origin in the kidney. The fact that constitutional susceptibility must be assumed to explain the development of hypertension by this mechanism is regrettable from the physiological standpoint, but is in accord with well supported clinical observations. It is consistent with the evidence that with depression of the secretion of the neural hypophysis there occurs a sensitization of the smooth musculature, including that of the blood vessels to epinephrine (Heinbecker, 1937) to adrenal cortical hormone and to renin (Heinbecker, unpublished data).

The implications of the concept of the pathogenesis of hypertension pertinent to our problem are that there are but two organs producing the hormones concerned in the causation of essential hypertension which can be modified by sympathectomy. These are the kidney and the adrenal gland. The results of anatomic investigations concerning the innervation of the kidney and the adrenal glands are in agreement in showing that the nerves to the adrenal gland and the kidney pass from the celiac ganglion and the upper two lumbar ganglia. The fibers which go to the celiac ganglion are derived from the three splanchnic nerves. Any operation which sections the splanchnic nerves prior to their junction with the celiac ganglion and the upper two lumbar ganglia must therefore effectively denervate the adrenal gland and the kidney.

The effect of a removal of sympathetic nerves more extensive than that outlined above can be only to temporarily enlarge the vascular bed under such sympathetic control. That the enlargement is temporary has been well established by the experimental work of Cannon (1932) and of others. After a period of time has elapsed, the arteries return to their normal calibre through the action of an intrinsic mechanism which is not nervous in character. Reflex narrowing of the denervated vessels is eliminated. This, however, for reasons stated is not deemed significant in the pathogenesis of essential hypertension.

The adrenal cortex is not directly innervated by the sympathetic nervous system. The adrenal medulla, on the other hand, is dependent upon sympathetic innervation for its secretory activity. Denervation of the adrenal medulla is regarded as of great significance in the treatment of essential hypertension. A decrease in the amount of its secretion is held to be responsible for the depression of the excitability of the central nervous system for influences which normally lead to a depression of the hypothalamus. The evidence in support of this concept is both experimental and clinical. Electroencephalographic studies in the cat, carried out in our laboratory, have shown that epinephrine has a profound excitatory influence on the activity of the central nervous system including the frontal lobe. The increased activity is demon-

strated by an increase in amplitude and frequency of the waves recorded from the surface of the brain (Heinbecker and Bartley, unpublished data) The effect of epinephrine on the isolated, spontaneously active ganglion cells on the limulus heart cord is to increase the frequency and the magnitude of the ganglion cell response (Heinbecker, 1933) The assumption is therefore made that a marked decrease in circulating epinephrine would lead to lessened irritability of the cells of the central nervous system, particularly those of the cerebral cortex

It must be admitted that hypertension may serve a useful purpose Even with the elevation in pressure the circulation to the various tissues of the body is not increased It is known that the flow to the kidneys may be decreased Only in the kidneys does there exist an intrinsic mechanism for increasing the blood pressure and thereby the renal blood flow Present evidence indicates that renin is released whenever the circulation to the renal tubules is decreased In extensive sympathectomy the temporary increase in the size of the vascular bed results frequently in a decrease in blood pressure without any increase in blood volume There is evidence that the cardiac output is decreased (Grimson, 1946) Because of these facts it follows that if the vascular narrowing in the kidneys is primarily humoral and non-nervous, the shunting of blood from the kidneys which must result from extensive sympathectomy would not only impair the renal function but also increase the release of renin which may be markedly injurious to the blood vessels of the body if sufficient in amount

The observation that operations for hypertension are more effective in the young than in the old can be explained on the basis that the narrowing of the arterioles in this stage of the hypertensive process is largely functional Inasmuch as the initiating mechanism responsible for the ultimate vascular narrowing has been stated as being in the central nervous system, it follows that any depression of its activity such as would be effected through denervation of the adrenals would depress the physiologic factors responsible for the hypertension Only when persons with hypertension are in the state where depression of the mechanism for hypertension can account for the depression of blood pressure which follows operations for hypertension are they justified The concept that hypertension *per se* is responsible for the degenerative changes of blood vessels is not supported by the experimental evidence Thus, Goldblatt (1947) has found that dogs made hypertensive by renal blood vessel clamping, even after six years of hypertension, do not show arteriolar sclerosis such as is seen at autopsy in human beings with essential hypertension The only significant change manifest in the arterioles of animals after prolonged hypertension is a thickening of the musculature of the arteriolar walls corresponding to the concentric muscular thickening of the left ventricle Changes which characterize the arteriolar sclerosis of essential hypertension are to be attributed to the metabolic disturbances initiated by overaction of the hormone of the eosinophil cells of the hypophysis acting in combination with the associated overactivity of the adrenal cortex The acute

degenerative changes in the arterioles found in the malignant phase of essential hypertension are reproducible in dogs when an excess of renin is released (Goldblatt, 1947, loc cit) From these facts it may be concluded that the lowering of blood pressure by the extensive denervation of the blood vessels cannot be expected to serve any useful purpose in preserving them from arteriolar sclerosis and denegeration

#### SUMMARY

Evidence is presented to establish that a humoral mechanism, not overaction of the sympathetic nervous system, is the primary cause of essential hypertension

A concept of the pathogenesis of essential hypertension is outlined. It is postulated on the basis of studies of Cushing's syndrome and of studies of hypothalamico-hypophysial relationships in the dog, that in man hypophysial eosinophil cell overaction with a resultant trophic stimulation of the adrenal cortex due to functional depression of the hypothalamic nuclei innervating the neural hypophysis is the primary cause of essential hypertension. The combined influence of the eosinophil cell—adrenal cortical hormone complex is to constrict the efferent glomerular arterioles of the kidney to result in a release of renin. The combined action of these three hormones causes hypertension and also the arteriolar sclerosis and degeneration ultimately associated with it. A constitutional susceptibility of the hypothalamus to depression and of the blood vessels to the constricting action of the hormones concerned in the causation of hypertension is deemed a prerequisite.

The role of epinephrine in hypertension is one of stimulation of the frontal lobes of the cerebral cortex. Its decrease by sympathectomy of the adrenal medulla is considered to be the mechanism whereby the production of hormones concerned in the pathogenesis of essential hypertension are decreased. Its decrease is responsible also in large measure for the relief from the symptoms of hypertension referable to the nervous system following sympathectomy of the adrenals.

Hypertension is regarded as a response of the body to a set of circumstances which threatens the adequate blood flow to the kidneys. A procedure is desirable only when it is capable of lessening the intensity of the humoral mechanism responsible for this deficiency of renal blood flow and when the consequent drop in blood pressure results from removal of the threatening circumstances rather than from an enlargement of the vascular bed.

In the treatment of hypertension the only two organs capable of releasing humors concerned with the pathogenesis and symptomatology of hypertension and whose function can be modified by sympathectomy are the kidneys and the adrenals. It follows that any beneficial effect to be obtained by removal of portions of the sympathetic nervous system in the treatment of essential hypertension is to be obtained when such removal results in a denervation of the adrenals and the kidneys.

The removal of portions of the sympathetic nervous system more extensive than is required for denervation of the adrenals and the kidneys is unnecessary. It can have no influence on the causal mechanism of essential hypertension. The temporarily greater enlargement of the vascular bed effected thereby may cause a shunting of blood from the kidneys sufficient to impair their function and thereby, through the release of renin, accelerate the degenerative changes in the extra-renal blood vessels.

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DISCUSSION—DR W. MCK. CRAIG, Rochester, Minn. In any consideration of the surgical treatment of hypertension it is apparent the causative factors must be kept in mind. Hypertension in the concept of Richard Bright was caused by kidney involvement, but Sir William Gull suggested that narrowing of the arterioles played an important role. Ever since that time the cause of hypertension has been controversial. Doctor Heinbecker has presented a logical and comprehensive argument in favor of a minimal surgical removal of the sympathetic nervous system, but in contrast to his argument there are

some convincing reports in the literature that more extensive portions of the sympathetic nervous system should be removed. The challenge which the surgical treatment of hypertension must accept is based on a graph designed by the combined researches of the interest and the ophthalmologist in which the various groups are portrayed with the life expectancy. The groups range from I to IV depending upon the severity of the disease.

Any successful treatment of hypertension should alter the prognosis of the disease as portrayed in the delineation of the four groups. If by surgical intervention we can change the course of any group we have accomplished something, for that in itself is an acknowledgment of a change in prognosis.

The removal of the subdiaphragmatic portion of the splanchnic nerves and the ganglionated trunk has accomplished something in the treatment of hypertension, but more extensive resections of the splanchnic nerves and ganglionated trunks are being done with gratifying and interesting results. Time will prove how much of the sympathetic nervous system will have to be removed in order to influence the ultimate course of the hypertensive patient.

DR PETER HEINBECKER, St. Louis (closing). I thank Doctor Craig for his discussion. I do not wish to leave the impression that I consider the adrenals and kidneys to be the only organs which have to do with hypertension. They are the only ones whose function can be modified by sympathectomy. Also, I do not agree that there is any necessity for a more extensive operation to denervate the adrenals and the kidneys than that originally described by Craig and Adson. When I analyze the reports of various operators in this field I can see no difference in their results, if we take into consideration the age of the patient and the age of the disease.

## THE PARADOX OF ACIDURIA IN THE PRESENCE OF ALKALOSIS CAUSED BY HYPOCHLOREMIA\*

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THE PARADOX OF ACID URINE excretion in the presence of internal alkalosis caused by loss of gastric juice is a phenomenon that has been recognized by a few investigators especially interested in the acid-base balance, but remains unfamiliar to most physicians. In this day of sulfonamide therapy and whole blood transfusions, with the accompanying increasing frequency of occasions when alkalinization of urine is considered desirable, it becomes pertinent to study the details of a condition in which a low urine pH does not indicate either the desirability or the safety of alkali administration.

An acid urine in the presence of internal alkalosis may be encountered whenever there is severe loss of gastric juice, as by vomiting or gastric suction. The paradoxical combination that results is a plasma of abnormally high pH and bicarbonate content, accompanied by a urine of low pH and practically no bicarbonate content.

The lost gastric juice contains both hydrochloric acid and chlorides of Na and K, chiefly Na<sup>1, 2</sup>. Loss of the sodium chloride and its equivalent of water causes dehydration. Loss of the hydrochloric acid causes part of the remaining plasma sodium chloride to be replaced by sodium bicarbonate, causing alkalosis to complicate the chloride loss and dehydration. In this condition, there is such a great depletion of body sodium salts that the kidneys cease to excrete sodium as either chloride or bicarbonate, despite the excessive plasma concentration of the bicarbonate. Urine lacking bicarbonate is acid<sup>3, 4</sup>. The condition encountered, therefore, is one in which an internal alkalosis, caused by loss of hydrochloric acid, is accompanied by excretion of acid urine.

As first noted by Haden and Orr in 1923,<sup>5</sup> bicarbonate administration in this condition is contraindicated because it increases the internal alkalosis and hastens the onset of tetany. If such a patient requires alkalinization of the urine, the preferable means is infusion of sodium chloride solution, this corrects the dehydration, sodium, and chloride deficit, decreases the internal alkalosis, and, at the same time, permits excretion of an alkaline urine, for alleviation of the body's deficit of sodium salts allows their excretion to be resumed. Of the excreted salts, part are in the form of bicarbonate, excreted from the excess present in the body, so that the urine pH rises. Sodium

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chloride infusion thus simultaneously alkalinizes the urine and restores the normal electrolyte pattern to the plasma and extracellular fluids of the body

The concurrence of alkalosis and acid urine was produced experimentally in dogs in 1924 by Gamble and Ross,<sup>2</sup> who made a detailed study of the plasma and urine electrolyte changes and clearly discussed their significance. Hartmann and Smyth in 1926<sup>6</sup> studied the condition as produced by vomiting in patients, noting the concurrence of bicarbonate excess and chloride deficit in the plasma accompanied by acid urine, they attributed the acidity of the urine to non-excretion of sodium bicarbonate, which, they believed, occurred when the total "concentration of crystalloids" in the plasma was diminished. Several other authors, quoted by McCance and Widdowson<sup>7</sup> have noted the phenomenon, but it still appears not to have attained general recognition or understanding.

The present work supplements that of Gamble and Ross by providing additional studies of the experimentally induced condition, together with hour-by-hour observation of the blood and urine changes caused by sodium chloride and by sodium bicarbonate infusions. Control experiments have been done in which sodium chloride and sodium bicarbonate solutions were infused into normal dogs.

#### EXPERIMENTAL

Loss of gastric juice was produced in dogs by two methods. By the total gastric pouch method of Dragstedt,<sup>8</sup> and by gastrostomy combined with ligation of the pylorus. At the time of the original operation, an episiotomy was performed to permit easy catheterization during periods of urine collection. Daily intravenous 5 per cent dextrose solutions were infused during the three to five days required for body chloride depletion. When the plasma chloride concentration fell to below 70 milliequivalents per liter (400 mg NaCl per 100 cc) the dogs were considered to be sufficiently depleted of chloride for this study. Moderate or severe alkalosis, as determined by abnormally high plasma bicarbonate concentration, was invariably produced.

The dogs were then given intravenous infusions of either 0.9 per cent NaCl or 1.3 per cent  $\text{NaHCO}_3$  at a constant rate of about 1000 cc per three hours. These solutions are, in electrolyte concentration, isotonic with plasma and contain 1.5 times the sodium concentration of normal plasma. However, the chloride content of the isotonic NaCl infusion is about 1.4 times that of normal dog plasma, and the bicarbonate concentration of the  $\text{NaHCO}_3$  infusion is about six times that of the normal plasma. In addition to these electrolytes, all infusions contained 5 per cent dextrose to stimulate the excretion of adequate urine volumes for chemical analyses.

Heparinized jugular venous blood samples were collected at 30-60 minute intervals throughout each experiment, the samples for  $\text{CO}_2$  analysis being taken under oil. Consecutive 15-30 minute period urine samples were collected from an indwelling catheter, with complete emptying of the bladder at the end of each period by air flushing except in experiments where urine was collected under oil for  $\text{CO}_2$  analyses. Nembutal sedation was used only when necessary.

The following analytic methods were employed plasma  $\text{CO}_2$  content by the manometric method of Van Slyke and Neill,<sup>9</sup> plasma and urine chlorides by Van Slyke and Hillel's modification of the titrimetric silver iodate method of Sendroy,<sup>10</sup> urine pH by glass electrode, plasma and urine sodium and potassium by the flame photometer constructed by the Perkin-Elmer Corporation,<sup>11</sup> total plasma base by the electrodialytic method of Malm (unpublished) based on the procedure of Adair and Keys,<sup>12</sup> plasma protein by the copper sulfate specific gravity method of Phillips et al.,<sup>13</sup> hematocrits by centrifugation

For presenting and plotting the results, values for chloride, bicarbonate, sodium, total base, potassium, and  $\text{R}^2$  are expressed in milliequivalents per liter of the ions,  $\text{Cl}$ ,  $\text{HCO}_3$ ,  $\text{Na}$ , etc., rather than in grams of their respective salts. The use of milliequivalents facilitates comparison of the concentrations and changes in the different electrolytes. Normal dog plasma contains about 150 to 158 mEq/L of total base, the distribution being about 140 mEq/L of  $\text{Na}$ , 5 of  $\text{Ca}$ , 5 of  $\text{K}$ , and 3 of  $\text{Mg}$ . These cations are balanced by 105 to 115 mEq/L of  $\text{Cl}$ , 20–25 of  $\text{HCO}_3$ , about 16 of protein, and the remainder by a residual sum, indicated by the symbol  $\text{R}$ , comprising  $\text{SO}_4$ ,  $\text{HPO}_4$ , and unidentified anions. The sum of  $\text{Cl} + \text{HCO}_3$  usually approximates the  $\text{Na}$ , except in starvation or dehydration when the  $\text{R}$  factor may be large. The only marked difference noted between the plasma electrolytes of man and the dog is that the chloride in the dog averages about 10 mEq/L higher than in man. The "isotonic" 0.9 per cent  $\text{NaCl}$  solution used for injections contains 154 mEq/L of  $\text{Na}$  and  $\text{Cl}$ , and the "isotonic" 1.3 per cent  $\text{NaHCO}_3$  contains 154 mEq/L of  $\text{Na}$  and of  $\text{HCO}_3$ .

The experiments presented below are selected as examples from 20 experiments that yielded similar results.

## RESULTS

With only two exceptions in 20 experiments (experiments 3 and 4 in this paper) all the hypochloremic dogs (46–65 mEq/L plasma chloride concentration) showed the paradox of aciduria (urine pH 5–6) in the presence of moderate to severe alkalosis (plasma  $\text{CO}_2$  35–51 mM/L). Infusion of solutions of either sodium chloride or sodium bicarbonate into such dogs increased the urine pH. Sodium chloride infusion raised the urine pH in some cases as high as 7.8. Sodium bicarbonate infusions raised it as high as 8.4. Little or no rise of urine pH occurred when a hypochloremic dog was given intravenous 5 per cent dextrose solution, and sodium chloride infusion into normal dogs caused a fall in urine pH.

### Experiment 1 The Effect of Infusing 0.9 Per Cent $\text{NaCl}$ + 5 Per Cent Dextrose Intravenously Into Hypochloremic Dog (Fig 1a, 1b, 1c, 1d, Table I)

This experiment was conducted four days after gastrotomy and pyloric ligation of a 43-pound dog. Plasma analyses (see Table I) immediately prior to the saline infusion showed the dog to be in a state of extreme hypochloremia (plasma  $\text{Cl}$  45.6 mEq/L), alkalosis (plasma  $\text{HCO}_3$  49.9 mEq/L),\* total base deficiency (plasma total base 137.3 mEq/L) and sodium deficiency (plasma sodium 125.5 mEq/L). Unfortunately, an

\*  $\text{HCO}_3$  concentrations in this paper are calculated from plasma  $\text{CO}_2$  measurements by assuming a plasma pH of 7.5.

adequate pre-infusion urine sample was not obtained, for the dog had a tetanic convulsion and emptied her bladder just before the infusion was begun. The preliminary urine was undoubtedly acid, for the urine pH was 5.3 an hour after the infusion was started and the urine of almost all other hypochloremic dogs was acid.

During a 12-hour period, 4670 cc of 0.9 per cent NaCl in five per cent dextrose solution was infused intravenously at a constant rate of 90–100 drops per minute. Small doses of intravenous nembutal controlled restlessness without putting the dog to sleep. Urine was collected in 30-minute periods under oil. Hourly jugular blood samples were also collected under oil. The infusion was continued 12 hours.

During the 12-hr infusion 2853 cc of urine were excreted (see Figure 1d), while 1817 cc, 38.9 per cent, of the infused water was retained. Of the 42 Gm of NaCl infused, 11 Gm were excreted and 31 Gm, or 74 per cent, were retained. 5.6 Gm of  $\text{NaHCO}_3$  (66.5 millimoles) were excreted during the experiment, this is equivalent to about 2.8 times the total grams of  $\text{NaHCO}_3$  in the plasma of a normal dog of this animal's weight, and more than even this alkalotic animal had in her plasma at the beginning of the infusion. Obviously a good deal of the excreted sodium bicarbonate came from the interstitial fluids.

Figures 1a and 1b and table I show in detail the manner in which the intravenous sodium chloride infusion corrected both the hypochloremia and the alkalosis caused by gastric fluid loss. There is a striking return of the plasma acid-base balance to normal. Plasma Cl concentration rose from 45.6 mEq/L to the normal 110.0 mEq/L. Plasma bicarbonate fell from 49.9 mM/L to 27.7 mM/L. Plasma total base rose from 137.3 mEq/L to 154.0 mEq/L and plasma sodium from 125.5 to 150.0 mEq/L. Undeterminable anions,\* Gambel's R factor<sup>2</sup> fell from 18.5 mEq/L to 3.1 mEq/L. During the last three hours of the infusion the hematocrit and the concentrations of protein, chloride, and bicarbonate in the plasma remained nearly constant at normal levels, indicating that the body's water and chloride deficits, and its bicarbonate excess, had been corrected.

The decrease in plasma bicarbonate concentration was partly due to the bicarbonate excretion discussed above, but in part it was attributable to dilution of the plasma and interstitial fluids with the infused 154 millimolar NaCl solution, which contained no bicarbonate and three times the plasma's Cl concentration. Dilution of the body's extracellular fluids with this chloride solution would obviously raise the Cl and lower the  $\text{HCO}_3$  concentration. This dilution effect is shown by the rise of Cl and fall of  $\text{HCO}_3$  in the plasma during the first three hours of the infusion, when practically no chloride or bicarbonate was being excreted.

Figures 1c and 1d and Table I show strikingly the way in which correcting the internal sodium chloride deficit released the excess bicarbonate for excretion, and in so doing raised the urine pH. When, after the third hour of infusion (1010 cc, 9 Gm NaCl), excretion of sodium salts began to be accelerated, the first salt to be excreted was not chloride, but bicarbonate (Fig. 1c). From the third to the seventh hour the urine contained more bicarbonate than chloride. Then, plasma chloride having been doubled and plasma bicarbonate lowered by a third (Fig. 1a), urinary chloride concentration began to surpass bicarbonate.

The effect of the rise in urine bicarbonate in raising urine pH is shown by the parallelism of the pH and  $\text{HCO}_3$  concentration curves in Figure 1c. Rise of urine bicarbonate concentration from 0.7 to its maximum of 44.1 millimoles per liter raised the pH from 5.3 to its maximum of 7.8. Thereafter, bicarbonate excretion continued in somewhat lower, but still rather high concentration, and urine pH continued at 7.42–7.68.

\* R factor, the undeterminable anions, is determined by subtracting the sum of base combined with Cl,  $\text{HCO}_3$ , and proteins from the total base. In these experiments the base combined with proteins is calculated  $B_{\text{protein}} = 0.234 \times \text{Gm per cent protein}$  assuming a normal A/G ratio of 1.8 (14). Total base determinations, by the electro-dialysis method employed, do not include  $\text{Mg}^{++}$ .

# ACIDURIA WITH ALKALOSIS

Chloride excretion was insignificant until the plasma chloride concentration reached 80 mEq/L. As the plasma chloride concentration rose above 80 mEq/L the rate of chloride excretion rose with it, the threshold level of plasma chloride was therefore about 80 mEq/L in this experiment

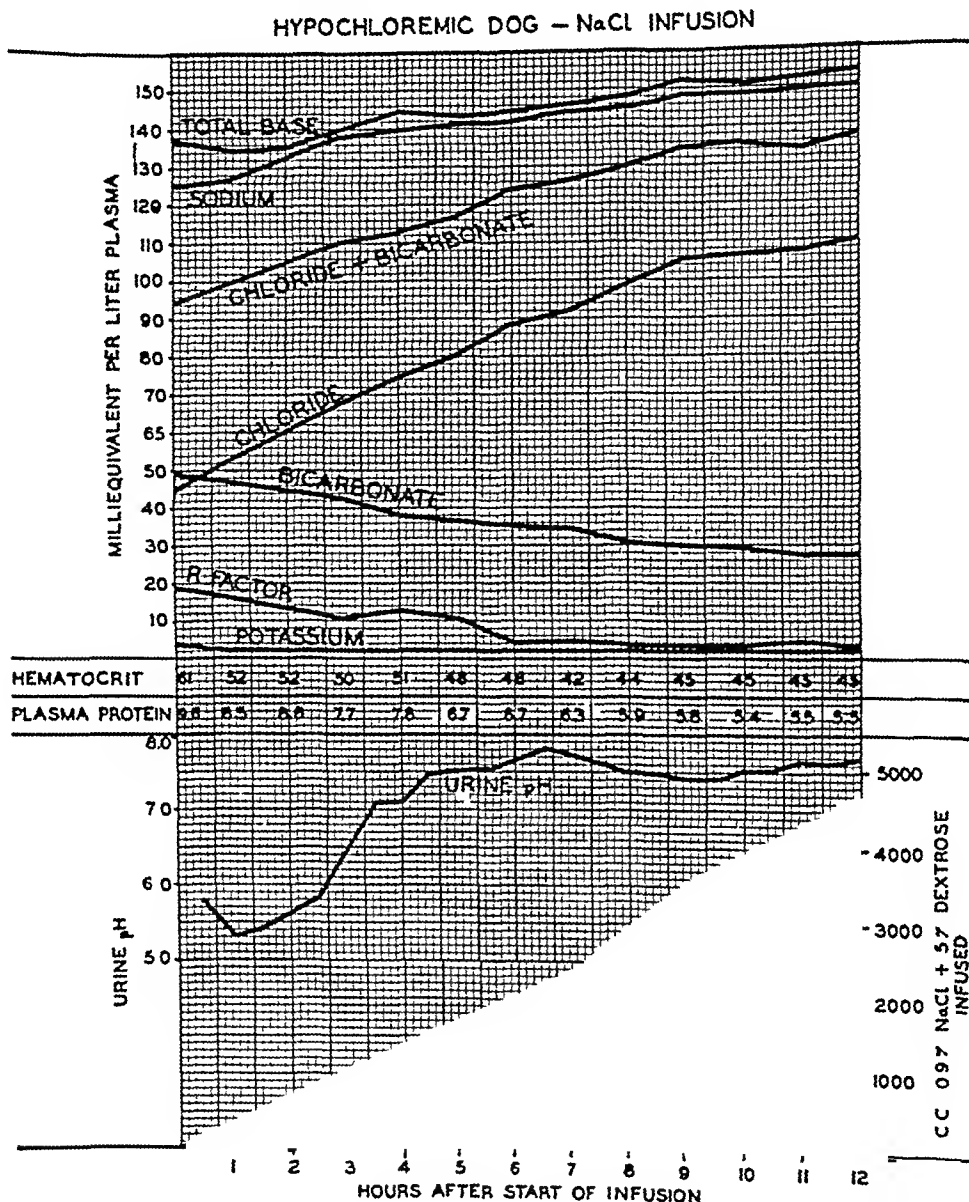


FIG 1A—Showing the effect of 0.9 per cent NaCl + 5 per cent dextrose infusion on the plasma electrolyte pattern of a hypochloremic alkalotic dog. Note that, despite the fall in plasma bicarbonate concentration the urine pH rises as the body NaCl deficit is corrected

At the start of this experiment the plasma *potassium* concentration was 3.9 mEq/L (normal 4.5–5.0 mEq/L). This potassium deficit is consistent with the observations of Gambel and McIver<sup>1</sup> that cat and dog gastric juice contains up to 50 mg per cent of potassium and with the observation of Elkinton and Winkler<sup>15</sup> that dehydration in itself is likely to diminish the potassium supply of the body

Within an hour after the start of the sodium chloride and dextrose infusion the plasma potassium fell to 2.0 mEq/L and thereafter it remained below 2.7 mEq/L. Similar washing out of plasma potassium by infused sodium chloride solution has been reported in experiments by Flock<sup>16</sup>, and recently Holler<sup>17</sup> and Martin and Wertman<sup>18</sup> have clinically observed reduction of plasma potassium to paralytic levels in diabetic

TABLE I  
H<sub>3</sub>POCHLOREMIC DOC  
0.9% NaCl+5% DEXTROSE I V INFUSION

Procedure			Plasma										
Minutes after start of infusion	Volume infused (cc)	NaCl infused (Gm.)	Blood and Urine Samples	Sample	Hemato-crit %	Total Protein Gm %	Cl mEq/L	HCO <sub>2</sub> mM/L	Cl+HCO <sub>3</sub> mEq/L	R	Na mEq/L	K mEq/L	Total base mEq/L
-15	0		Bc Uc	Bc	60.5	9.61	45.6	49.9	95.5	18.5	125.5	3.9	137.3
0	0		Uc										
30	200	1.8	U1	B1	52.2	8.50	53.6	lost			127.5	2.0	134.9
60	360	3.2	U2										
90	615	5.5	U3	B2	52.4	8.61	60.5	lost			133.0		135.7
120	700	6.3	U4										
150	850	7.6	U5	B3	50.4	7.73	68.2	42.8	111.0	10.2	138.5	2.1	140.0
180	1010	9.1	U6										
210	1180	10.6	U7	B4	51.3	7.80	75.0	38.3	113.3	12.6	140.0	2.1	144.8
240	1360	12.2	U8										
270	1500	13.5	U9	B5	47.5	6.67	80.0	36.9	116.9	10.4	141.5	2.7	143.5
300	1680	15.1	U10										
330	1860	16.7	U11	B6	47.5	6.67	88.8	35.3	124.1	4.0	142.0	2.2	144.3
360			U12										
390	2190	19.7	U13	B7	46.5	6.28	92.0	34.4	126.4	4.5	144.5	2.5	146.2
420	2370	21.3	U14										
450	2680	24.1	U15	B8	43.8	5.90	99.0	30.8	129.8	3.7	145.5	2.2	147.8
480	2940	26.4	U16										
520			U17	B9	44.9	5.83	105.5	29.1	134.6	3.6	148.5		152.4
550	3520	31.7	U18										
570	3660	32.9	U19	B10	44.6	5.35	106.5	29.0	135.5	3.2	148.5	2.2	151.7
600	3870	34.8	U20										
630	4130	37.1	U21	B11	44.5	5.54	107.1	27.4	134.5	4.6	149.0	2.2	152.6
660	4290	38.6	U22										
690	4470	40.2	U23	B12	44.7	5.50	110.0	27.7	137.7	3.1	150.0	2.2	154.0
720	4670	42.0	U24										

TABLE I (cont.)  
HYPOCHLOREMIC DOG  
0.9% NaCl+5% DEXTROSE I V INFUSION  
Urine

Sample	Volume		pH	Chloride		NaCl Excretion mg/period	Sodium		HCO <sub>3</sub>			NaHCO <sub>3</sub> Excretion mg/period
	cc /period	cc /min		Concen- tration mEq/L	Excretion mEq/min		Concen- tration mEq/L	Excretion mEq/min	CO <sub>2</sub> mM/L	Concen- tration mEq/L	Excretion mEq/Min	
Uc	3											
U <sub>1</sub>	15	0.50	5.9	0	0	0	4	0.002	1.9	0.7	0.0	1
U <sub>2</sub>	41	1.36	5.3	0	0	0	4	0.005	1.4	0.2	0.0	1
U <sub>3</sub>	54	1.80	5.4	0.5	0.001	2	13	0.023				
U <sub>4</sub>												
U <sub>5</sub>	152	2.54	5.8	0.5	0.001	4	17	0.043	1.8	0.6	0.002	10
U <sub>6</sub>	96	3.20	6.4	0.5	0.002	4	26	0.083	5.2	3.5	0.001	28
U <sub>7</sub>	93	3.10	7.1	1.5	0.005	8	39	0.121				
U <sub>8</sub>	119	3.97	7.1	3.0	0.012	21	48	0.190	26.3	23.9	0.095	425
U <sub>9</sub>	103	3.44	7.45	3.4	0.012	21	48	0.165				
U <sub>10</sub>	116	3.87	7.54	5.6	0.022	38	52	0.201	32.9	31.6	0.122	582
U <sub>11</sub>	130	4.34	7.56	14.2	0.062	76	65	0.282				
U <sub>12</sub>	148	4.94	7.65	26.5	0.131	231	70	0.345	40.2	38.9	0.194	910
U <sub>13</sub>	66	2.20	7.80	36.8	0.081	142	74	0.163				
U <sub>14</sub>	100	3.33	7.76	42.2	0.147	246	78	0.252	45.0	44.1	0.147	616
U <sub>15</sub>	125	4.13	7.63	57.2	0.236	418	87	0.363				
U <sub>16</sub>	206	6.87	7.50	68.0	0.467	806	87	0.598	26.4	25.2	0.175	702
U <sub>17</sub>	172	4.30	7.49	89.5	0.385	900	94	0.404				
U <sub>18</sub>	318	10.60	7.42	115.0	1.220	2140	104	1.110	20.4	19.5	0.207	803
U <sub>19</sub>	92	4.60	7.43	118.5	0.543	638	130	0.598				
U <sub>20</sub>	157	5.24	7.52	121.9	0.639	1119	144	0.754	20.9	20.1	0.105	421
U <sub>21</sub>	132	4.40	7.54	124.3	0.547	959	152	0.669				
U <sub>22</sub>	136	4.54	7.68	128.5	0.584	1022	152	0.690	23.2	22.5	0.102	507
U <sub>23</sub>	144	4.80	7.61	130.0	0.624	1095	152	0.730				
U <sub>24</sub>	135	4.50	7.65	134.0	0.643	1113	152	0.684	25.3	24.6	0.106	577
	2853 cc					11.0 Gm						5.6 Gm

patients treated with large infusions of intravenous dextrose and sodium chloride. It is possible that some of the potassium is deposited into the liver and muscle with glycogen formed from the infused dextrose, as postulated by Fenn<sup>19</sup>

That paralysis did not develop may be due to the simultaneous loss of calcium. Though direct calcium determinations were not made in this experiment, the difference between total base and the  $\text{Na} + \text{K}$  in the plasma during the infusion fell so low that it appears that calcium must have fallen much below the normal 5 mEq/L. Since neither tetany nor paralysis occurred, the possibility suggests itself that simultaneous calcium

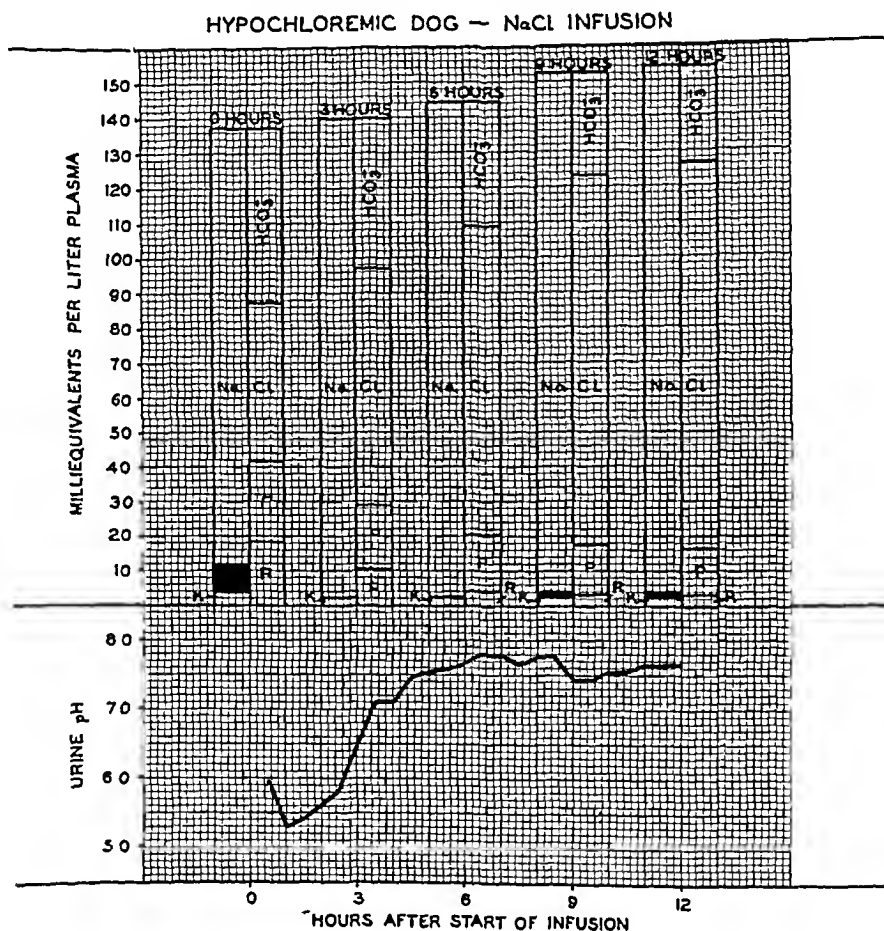


FIG 1B—Showing the effect of 0.9 per cent NaCl + 5 per cent dextrose infusion on the plasma electrolyte pattern of a hypochloremic alkalotic dog. Note that, despite the fall in plasma bicarbonate concentration, the urine pH rises as the body NaCl deficit is corrected. Also note the decrease in concentrations of cations other than sodium.

and potassium deficiency neutralized each other with regard to effect on muscle tone.

From this experiment, and from the clinical observations of others, it would seem advisable that a balanced electrolyte solution containing not only Na, but also Ca, K and Mg should be used when large electrolyte infusions are given.

This 43-pound dog excreted 5.6 Gm of  $\text{NaHCO}_3$  during the 12 hr NaCl solution infusion. This bicarbonate excretion is equivalent to about 20 Gm for a 70-kg man. Since the body contained at least this much excess bicarbonate, it is apparent that bicarbonate administration was not indicated, despite the acid urine.

**Experiment 2 The Effect of Infusing 0.9 Per Cent NaCl + 5 Per Cent Dextrose Intravenously Into Hypochloremic Dog (Fig 2, Table II)**

This experiment practically duplicates the first three hours of Experiment 1, except that the initial plasma chloride deficit and bicarbonate excess were not quite so great (Cl 56.6 mEq/L,  $\text{HCO}_3^-$  37 mM/L, compared with Cl 45.6 and  $\text{HCO}_3^-$  49.9 in Experiment 1, sum of chloride plus bicarbonate nearly the same in both) The infusion, as that of the

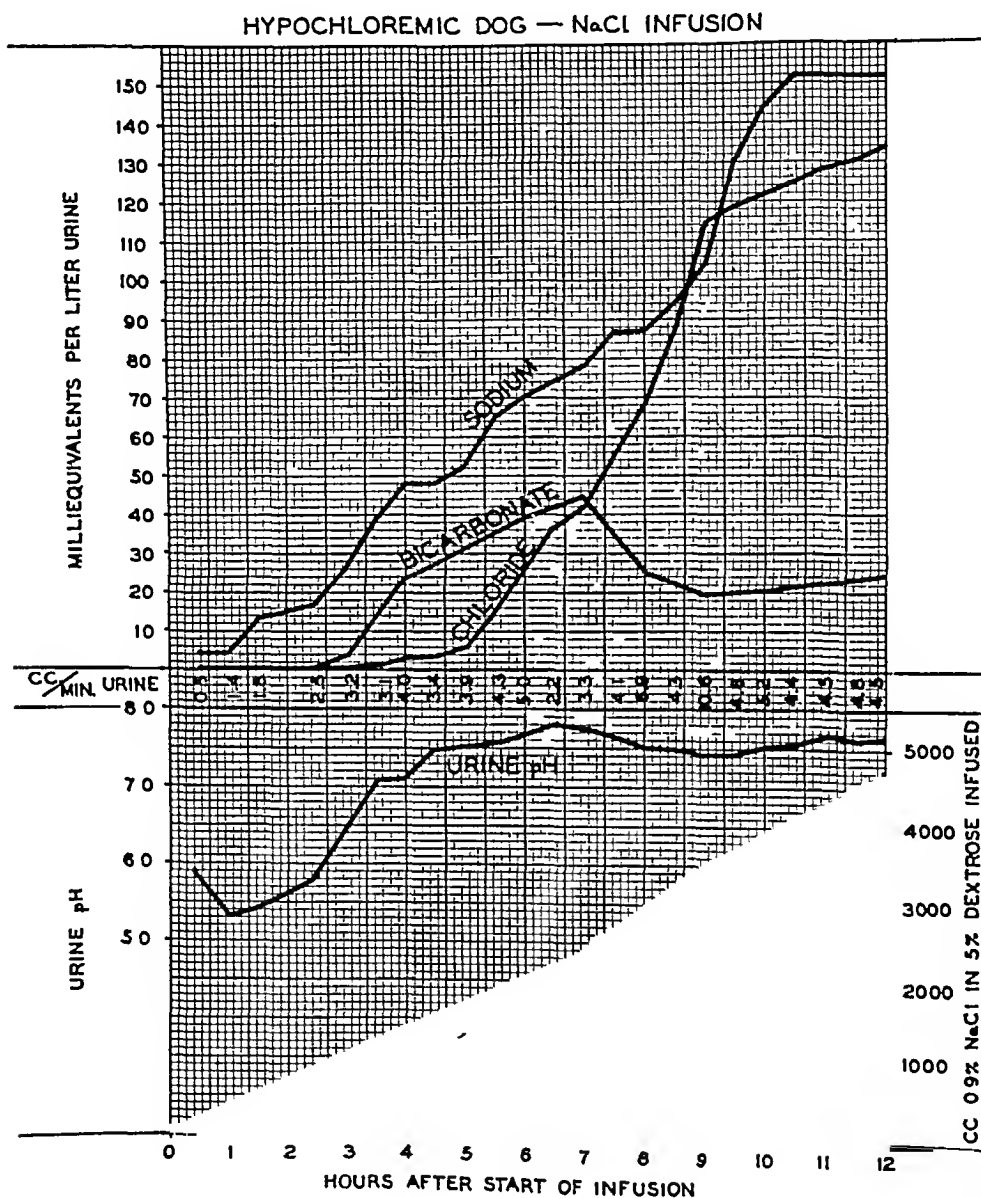


FIG 1C—Showing the effect of 0.9 per cent NaCl + 5 per cent dextrose infusion on the urine NaCl and  $\text{NaHCO}_3$  concentrations of a hypochloremic alkalotic dog. Note that NaCl infusion frees a large amount of  $\text{NaHCO}_3$  for excretion, and that urine pH parallels urine  $\text{NaHCO}_3$  concentration.

first three hours of dog one, was insufficient to start significant excretion of water, chloride, or bicarbonate, the urinary  $\text{HCO}_3^-$  concentration at the end of the three hours being sufficient only to raise the pH to 6.52. The initial dehydration of the dog is shown by the fact that during the three hours only eight per cent of the infused water was excreted. The partial correction of the plasma electrolyte picture (fall in  $\text{HCO}_3^-$ , rise in Cl and Na) is attributable, as in the first three hours of Experiment 1, to dilution of plasma and interstitial fluids with the infused 154 millimolar NaCl solution.



TABLE II  
HYPOCHLOREMIC DOG  
0.9% NaCl+5% DEXTROSE I V INFUSION

Procedure		Plasma				
Minutes After Start of Infusion	Volume Infused (cc)	Blood and Urine Samples	Sample	Hematocrit	CO <sub>2</sub> mM/L	Cl mEq/L
0	0	Bc Uc	Bc		39.5	56.6
35	160	B <sub>1</sub>	B <sub>1</sub>	25	35.4	61.3
60	260	B <sub>2</sub> U <sub>1</sub>	B <sub>2</sub>	24	34.7	62.3
90	400	B <sub>3</sub>	B <sub>3</sub>	20	34.2	65.8
120	570	B <sub>4</sub> U <sub>2</sub>	B <sub>4</sub>	19	32.0	69.4
150	760	B <sub>5</sub>	B <sub>5</sub>	22	33.6	73.3
180	890	B <sub>6</sub> U <sub>3</sub>	B <sub>6</sub>	21	31.0	76.0
						CO <sub>2</sub> +Cl mEq/L
						96.2
						96.7
						97.0
						100.0
						101.4
						106.9
						106.0
						Na mEq/L
						111
						111
						109
						112
						114
						116
						116

Urine		Sodium	
Sample	pH	Chloride	Excretion
		Concentration Gm/L	mg/min
Uc	5.97	0	0
U <sub>1</sub>	6.10	0	0.006
U <sub>2</sub>	6.00	0	0.023
U <sub>3</sub>	6.52	0.04	0.031
67 cc		10.8 mg	1.56 mg

Volume		CO <sub>2</sub>	
Sample	cc/period	Concentration Gm/L	mM/L
		Excretion Mg/min	mg/min
Uc	12	0	2.68
U <sub>1</sub>	0.20	0	2.28
U <sub>2</sub>	0.30	0	2.18
U <sub>3</sub>	0.62	0.026	3.70

# ACIDURIA WITH ALKALOSIS

Experiment 2 serves for comparison with Experiment 3 in which isotonic  $\text{NaHCO}_3$  instead of  $\text{NaCl}$  was infused. In both experiments the initial dehydration, plasma  $\text{Cl}$  deficit and  $\text{HCO}_3$  excess were nearly the same.

## Experiment 3 The Effect of Infusing 13 Per Cent $\text{NaHCO}_3$ + 5 Per Cent Dextrose Intravenously Into Hypochloremic Dog (Fig 3, Table III)

In this experiment a salt depleted dehydrated dog was infused with an isotonic solution of sodium bicarbonate instead of sodium chloride. 900 cc of 13 per cent sodium bicarbonate in five per cent dextrose solution were given during a three-hour period.

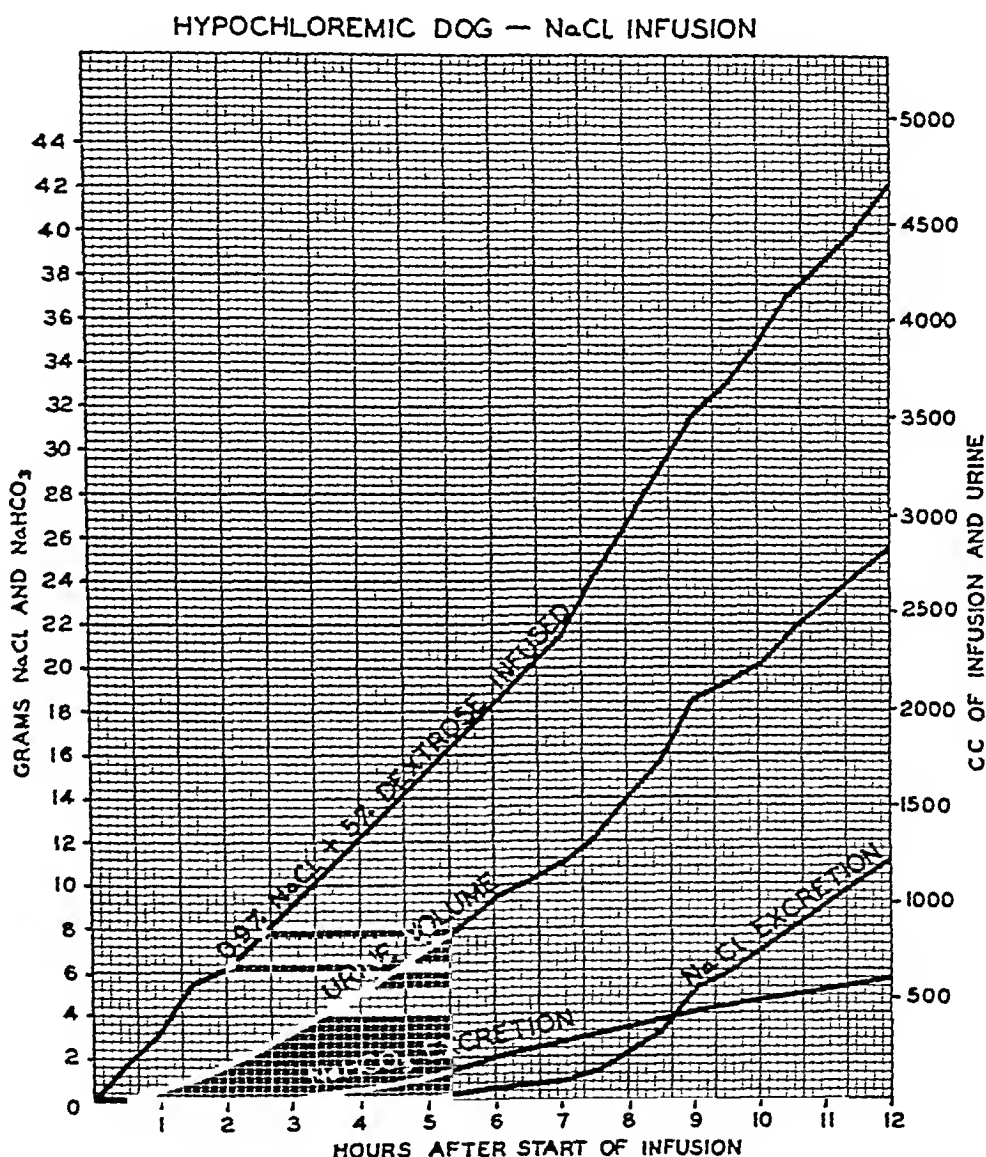


FIG 1D—Showing the total grams of  $\text{NaCl}$  and  $\text{NaHCO}_3$  excreted by a hypochloremic alkalotic dog receiving intravenous 0.9 per cent  $\text{NaCl}$  + 5 per cent dextrose. Note that  $\text{NaCl}$  infusion frees a large quantity of  $\text{NaHCO}_3$  for excretion.

Water excretion was more accelerated than in the previous experiments, the total urine excretion being 73 per cent of the infused solution, compared with eight per cent in Experiment 2. The diuresis was accompanied by a rapid increase in sodium salt excretion. The sodium excretion here was almost chloride free. The high bicarbonate content of the urine raised the pH above eight during most of the experimental period.

In this experiment, with sodium bicarbonate infusion, the infused sodium salt and water were less completely retained than in the preceding experiments where sodium chloride solution was infused. Of the sodium chloride infused during the previous experiments, only 0.0 to 0.1 per cent was excreted whereas of the sodium bicarbonate infused in this experiment, 38 per cent was excreted before the experiment finished.

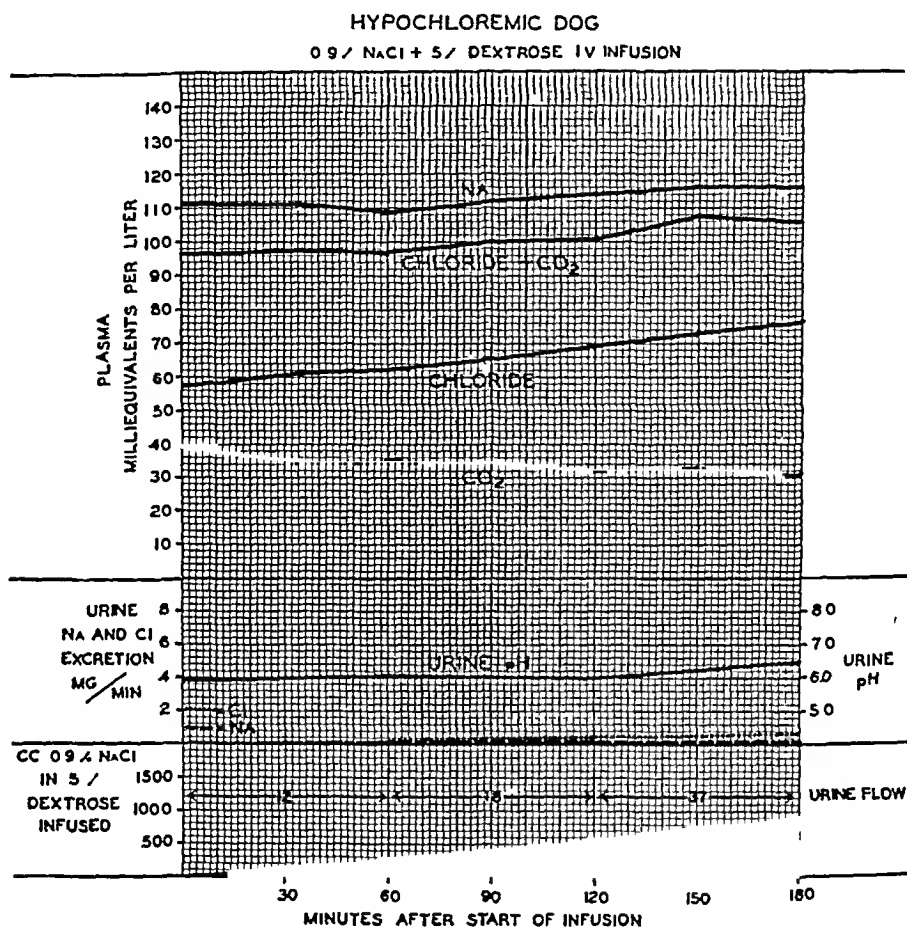


FIG 2—Showing the early effects of 0.9 per cent NaCl + 5 per cent dextrose infusion into a hypochloremic alkalotic dog. Note the almost complete retention of the infused saline causing plasma electrolyte changes by simple dilution and no changes in the urine.

It appears that the refusal of the kidneys to retain the infused bicarbonate may be attributable to the fact that the plasma bicarbonate concentration had already been raised by gastric hydrochloric acid loss to twice the normal level, and retention of bicarbonate would have increased the excess of that salt already present in the alkalotic organism.

The hypochloremic alkalotic plasma electrolyte pattern became even more marked during the bicarbonate infusion, chloride concentration fell, CO<sub>2</sub> rose, total base and R factor changed little. Thus the electrolyte imbalance was aggravated. This increasing alkalosis was accompanied by repeated convulsions necessitating intravenous nembutal.

The results indicate the undesirability of infusions of sodium bicarbonate in the state of hypochloremic alkalosis, even when accompanied by an initially acid urine.

TABLE III  
HYPOCHLOREMIC DOG  
1.3%  $\text{NaHCO}_3$ +5% DEXTROSE I V INFUSION

Minutes after Start of Infusion	Procedure		Blood and Urine Samples		Sample	Hematocrit %	Total Protein Gm %	Plasma					R
	Volume Infused (cc)		Bc	Uc				Cl mEq/L	HCO <sub>3</sub> mEq/L	Cl +HCO <sub>3</sub> mEq/L	Total Base mEq/L		
0	0		Bc	Uc	Bc	58.4	7.8	60.1	34.2	94.3	129.2	15.9	
30				U <sub>1</sub>									
45	200		B <sub>1</sub>		B <sub>1</sub>	52.5		55.0	40.7	95.7			
60				U <sub>2</sub>									
65	310		B <sub>2</sub>		B <sub>2</sub>	52.0		51.8	42.2	97.0			
90	420			U <sub>3</sub>									
95			B <sub>3</sub>		B <sub>3</sub>	48.7	6.2	52.9	41.6	94.5	129.5	19.9	
120	600			U <sub>4</sub>									
127			B <sub>4</sub>		B <sub>4</sub>	48.3	5.9	52.6	47.0	99.6	128.2	14.3	
150	750			U <sub>5</sub>									
165			B <sub>5</sub>		B <sub>5</sub>	48.9	6.0	51.9	48.4	100.3	131.2	16.3	
180	900		B <sub>6</sub>		B <sub>6</sub>	50.4	5.8	53.0	50.9	103.9	129.4	11.4	

Sample	Volume		pH	Chloride			Sodium			HCO <sub>3</sub>		Total NaHCO <sub>3</sub> Excretion Gm /period
	cc /period	cc /min		Concentration mEq/L	Excretion mEq/min	Excretion mg /period	Concentration mEq/L	Excretion mEq/min	CO <sub>2</sub> mM/L	Concentration mM/L	Excretion mM/min	
Uc			6.40	0	0	0	8.7		2.2	1.1		
U <sub>1</sub>	95	3.17	7.53	0	0	0	57.4	0.182	35.3	34.0	0.108	0.27
U <sub>2</sub>	98	3.27	8.08	1.1	0.004	6.3	74.4	0.243	71.3	70.5	0.230	0.58
U <sub>3</sub>	111	3.70	7.89	0.9	0.003	5.9	78.3	0.290	43.9	43.2	0.169	0.40
U <sub>4</sub>	146	4.87	8.02	1.2	0.006	10.3	98.3	0.479	73.6	72.7	0.354	0.89
U <sub>5</sub>	113	3.77	8.11	2.2	0.008	14.6	118.2	0.446	99.3	98.5	0.371	0.94
U <sub>6</sub>	98	3.27	8.16	2.3	0.008	13.2	130.5	0.427	165.1	164.7	0.538	1.36
	661 cc					50.3 mg						4.4Gm

TABLE IV  
HYPOCHLOREMIC DOG  
5% DEXTROSE IN WATER I V INFUSION

Minutes After Start of Infusion	Procedure Volume Infused (cc)	Blood and Urine Samples	Plasma				Sodium	
			Sample	Hematocrit	Cl mEq/L	CO <sub>2</sub> mM/L	Cl+CO <sub>2</sub> mM/L	Na mEq/L
0	0	Be U <sub>c</sub>	B <sub>c</sub>	45.7	64.6	40.1	104.7	120
25	110	B <sub>1</sub> U <sub>1</sub>	B <sub>1</sub>	43.2	61.0	39.4	100.4	115
60	290	B <sub>2</sub> U <sub>2</sub>	B <sub>2</sub>	42.0	58.6	37.2	95.8	112
90	430	B <sub>3</sub> U <sub>3</sub>	B <sub>3</sub>	40.8	57.4	35.0	92.4	109
120	620	B <sub>4</sub> U <sub>4</sub>	B <sub>4</sub>	41.8	56.4	37.9	94.3	103
150	790	B <sub>5</sub> U <sub>5</sub>	B <sub>5</sub>	54.9	54.9	37.5	92.4	
180	910	B <sub>6</sub> U <sub>6</sub>	B <sub>6</sub>	39.0	54.1	37.7	91.8	103

URINE		Chloride		Sodium	
Sample	pH	cc /period	Volume cc /min	Gm /L Concentration	mg /period Excretion
U <sub>c</sub>	6.72	16	0.64	0.025	0.03
U <sub>1</sub>	6.51	58	1.7	0.030	0.050
U <sub>2</sub>	6.54	45	1.5	0	<0.010
U <sub>3</sub>	6.90	88	2.9	0.014	<0.010
U <sub>4</sub>	6.90	61	2.0	0.007	<0.010
U <sub>5</sub>	7.15	51	1.8	0.007	<0.010
U <sub>6</sub>	7.19	—	—	0.019	<0.010
322 cc				5.6 mg	

TABLE V  
NORMAL DOG  
0.9% NaCl+5% DEXTROSE I V INFUSION

Procedure				Plasma			
Sample	Minutes After Start of Infusion	Volume Infused (cc)	Blood and Urine Samples	Hematocrit %	Total Protein Gm %	Cl mEq/L	Cl+CO <sub>2</sub> mEq/L
Uc	0	0	Bc Uc	33.9	4.34	103.0	125.9
U <sub>1</sub>	30	190	B <sub>1</sub> U <sub>1</sub>	33.8	4.26	108.3	131.8
U <sub>2</sub>	69	330	B <sub>2</sub> U <sub>2</sub>	33.7	4.15	110.5	133.1
U <sub>3</sub>	90	480	B <sub>3</sub> U <sub>3</sub>	33.6	4.08	112.5	134.4
U <sub>4</sub>	120	670	B <sub>4</sub> U <sub>4</sub>	33.0	4.04	114.5	134.8
U <sub>5</sub>	150	840	B <sub>5</sub> U <sub>5</sub>	33.1	3.90	116.5	134.5
U <sub>6</sub>	180	980	B <sub>6</sub> U <sub>6</sub>	33.2	3.90	117.6	135.1

URINE				Sodium				NaHCO <sub>3</sub>		NaHCO <sub>3</sub> Excretion mg /period
Sample	Volume cc /period	pH	Chloride Gm/L	mg/min Excretion	NaCl Excretion mg /period	Gm/L Concentration	mg/min Excretion	CO <sub>2</sub> mM/L	Gm/L Concentration	
Uc	32	1.07	2.4	2.57	41.4	1.4	1.50	4.9	0.29	0.31
U <sub>1</sub>	41	1.37	0.6	0.82	24.2	0.2	0.27	1.72	0.04	0.06
U <sub>2</sub>	18	0.60	0.8	0.48	106.1	0.1	0.06	1.08	0.03	0.02
U <sub>3</sub>	14	0.47	4.6	2.16	253.0	0.9	0.42	0.81	0.02	0.01
U <sub>4</sub>	20	0.66	7.7	5.08	391.0	2.3	1.52	0.78	0.00	0.00
U <sub>5</sub>	30	1.00	7.9	7.90	699.0	2.7	2.70	0.74	0.00	0.00
U <sub>6</sub>	79	2.63	5.3	13.92		1.5	3.95	0.96	0.00	0.00
										2.9 mg
										2.9 mg

**Experiment 4 The Effect of Infusing 5 Per Cent Dextrose In Water Into Hypochloremic Dog (Fig 4, Table IV)**

This experiment serves as control for those in which  $\text{NaCl}$  plus dextrose or  $\text{NaHCO}_3$  plus dextrose was infused. The dog received 910 cc of solution in three hours and excreted 322 cc of urine, or 35 per cent of the infused volume. The effects on plasma  $\text{Cl}$ ,  $\text{HCO}_3$  and  $\text{Na}$  concentrations are those of simple dilution by the retained water (hematocrit fell from 45.7 to 39.0 per cent). Excretion of  $\text{Cl}$  and  $\text{Na}$  were negligible. The urinary pH was raised only 0.4.

This control experiment shows that the rise in urine pH in Experiments 1, 2, and 3 was not the result of the glucose diuresis.

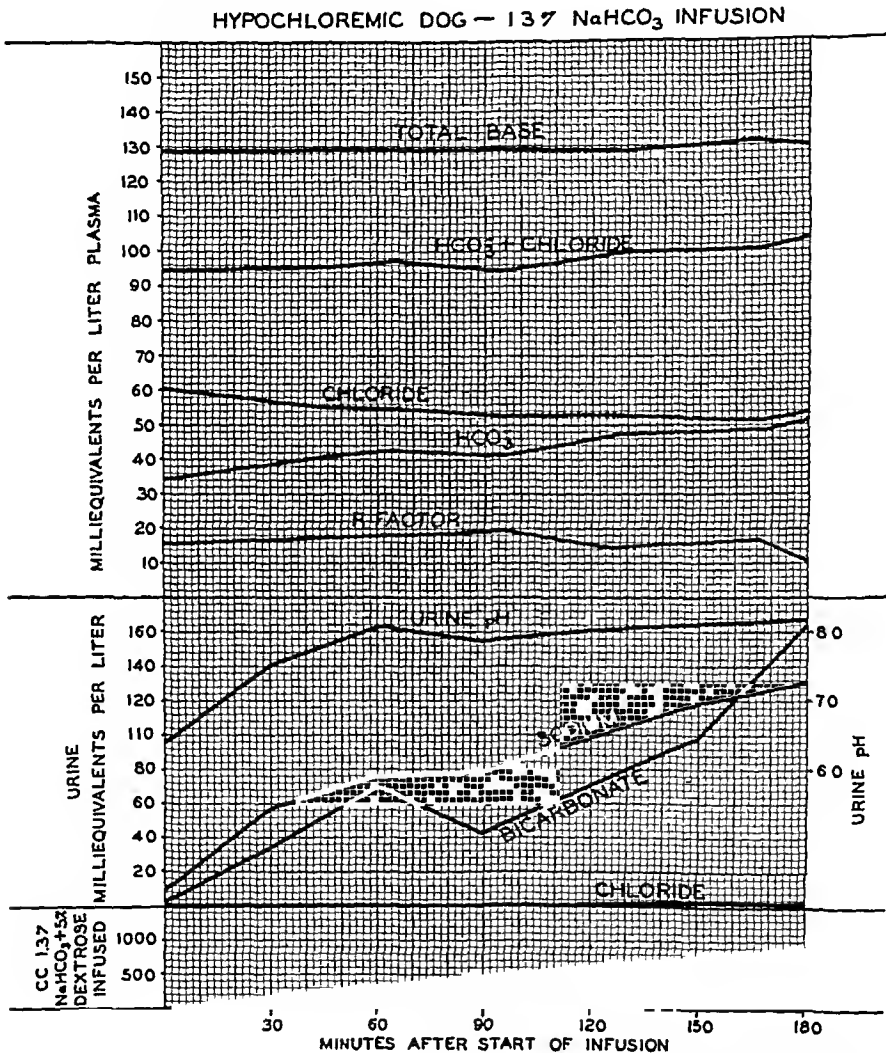


FIG 3—Showing the effects of 13 per cent (isotonic)  $\text{NaHCO}_3$  + 5 per cent dextrose infusion into a hypochloremic alkalotic dog (compare with Fig 2). Note the undesirable aggravation of the plasma anion imbalance and the failure to retain the infused solution.

This experiment shows (1) that dextrose solution infused without salt into a dehydrated animal is not well retained (35 per cent of infused fluid was excreted during the three-hour infusion compared with eight per cent when 0.9 per cent  $\text{NaCl}$  was infused), (2) that such infusion does not correct the plasma chloride deficit nor, to a

TABLE VI  
NORMAL DOG  
1.3% NaHCO<sub>3</sub> 5% DEXTROSE I V INFUSION

Procedure			Plasma			
Minutes after Start of Infusion	Volume Infused (cc)	Blood and Urine Samples	Hematocrit %	Cl mEq/L	Cl mM/L	Cl+CO <sub>2</sub> mEq/L
0	0	Bc Uc	32.7	116.0	23.6	139.6
60	360	B <sub>1</sub> U <sub>1</sub>	29.3	109.8	28.5	138.3
120	680	B <sub>2</sub> U <sub>2</sub>	29.5	107.3	35.1	142.4
187	1020	B <sub>3</sub> U <sub>3</sub>	30.5	104.1	38.7	142.8
240	1270	B <sub>4</sub> U <sub>4</sub>	30.4	104.1	37.6	141.7
300	1570	B <sub>5</sub> U <sub>5</sub>	29.3	102.2	38.2	140.6
340	1770	B <sub>6</sub> U <sub>6</sub>	28.9	102.5	40.7	143.2

URINE									
Chloride			Sodium			HCO <sub>3</sub>			
Sample	Volume cc/period	cc/min	Gm/L Concentration	mEq/min Excretion	mg/period Excretion	CO <sub>2</sub> mM/L	gm/L Concentration	mEq/min Excretion	NaHCO <sub>3</sub> Excretion mg/period
Uc	16	0.27	3.6	0.03	93.5	22.8	8.2	0.03	180
U <sub>1</sub>	70	1.17	2.4	0.08	272	136	10.9	0.21	1050
U <sub>2</sub>	143	2.14	1.7	0.10	395	140	8.5	0.30	1670
U <sub>3</sub>	220	4.16	1.4	0.16	500	141	8.5	0.58	2440
U <sub>4</sub>	252	4.20	1.2	0.15	492	143	8.6	0.60	3030
U <sub>5</sub>	173	4.33	0.74	0.09	207	154	9.3	0.66	2220
874 cc			1.86 Gm			10.6 Gm			



# HYPOCHLOREMIC DOG - DEXTROSE INFUSION

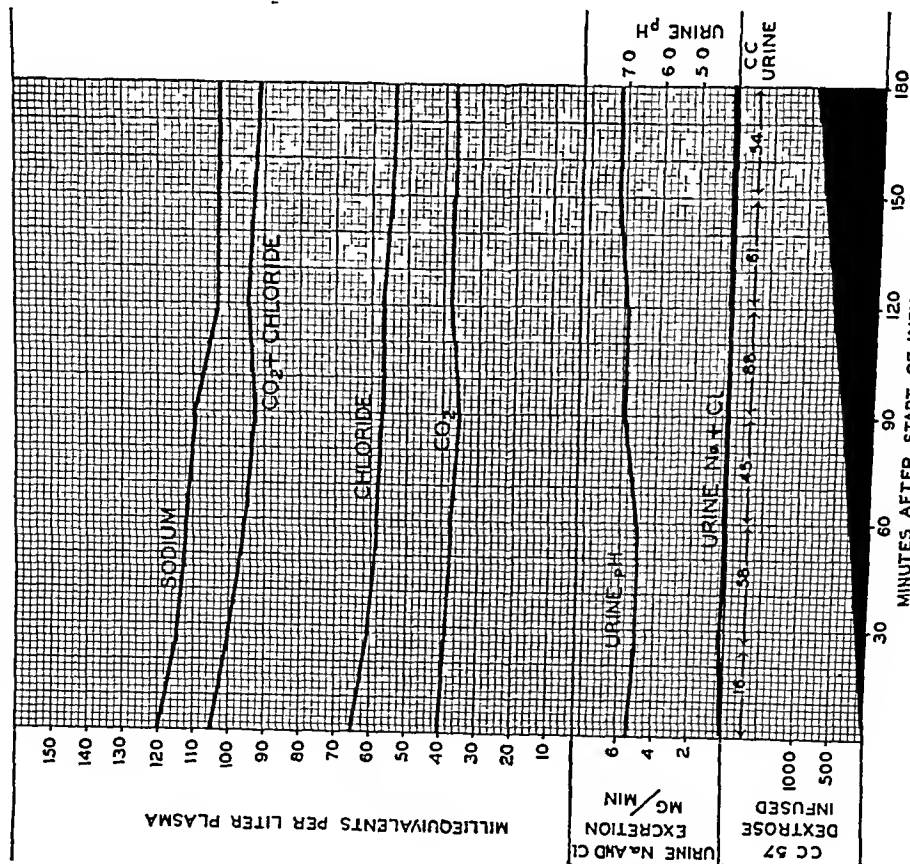


Fig 4—Control experiments showing the effects of five per cent dextrose infusion into a hypochloremic alkalotic dog. Note that the resultant diuresis does not raise the urine pH, and that the urinary effects of the NaCl dextrose and NaHCO<sub>3</sub> dextrose infusions in Experiments 1, 2, and 3 are not attributable to the infused dextrose

# NORMAL DOG - NaCl INFUSION

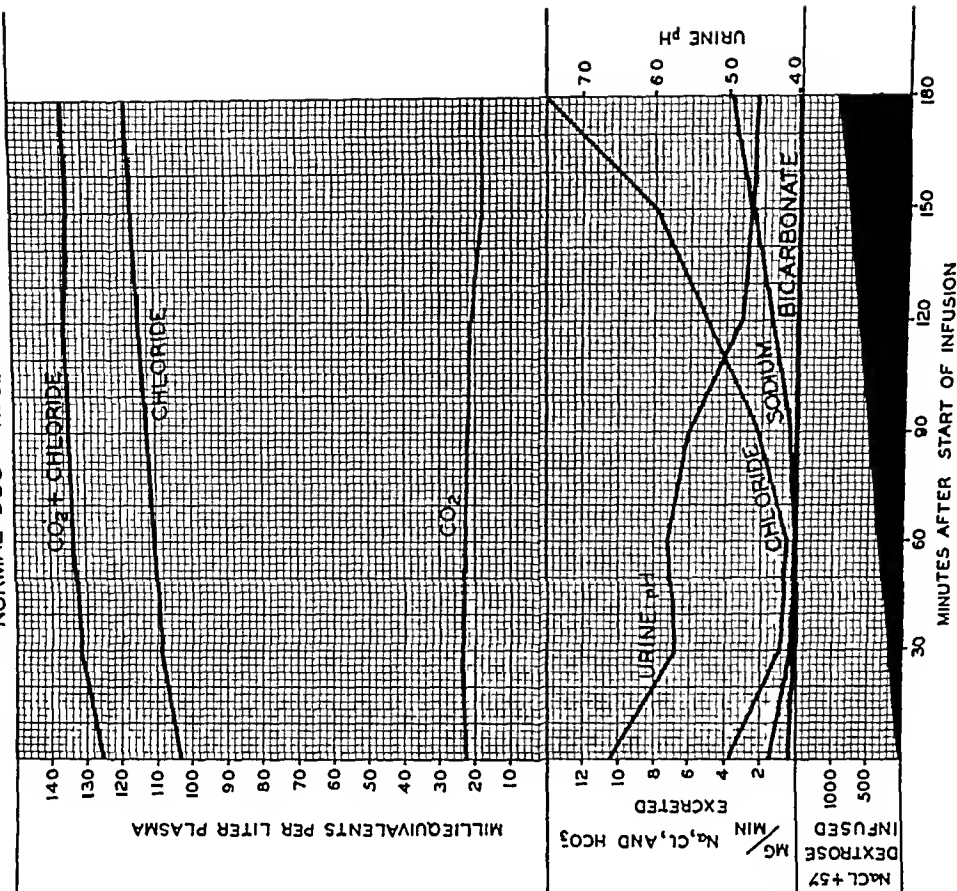


Fig 5—Control experiment showing the effects of 0.9 per cent NaCl + 5 per cent dextrose infusion into a normal dog. Compare with Figures 1, 2, and 3. Note the fall in urine pH caused by a dilution of the plasma bicarbonate to below its renal threshold concentration

ACIDURIA WITH ALKALOSIS

significant extent, the bicarbonate excess, and (3) that it does not accelerate bicarbonate excretion sufficiently to cause a marked rise in urinary pH

Experiment 5 The Effect of Infusing 0.9 Per Cent NaCl + 5 Per Cent Dextrose Into Normal Dog (Fig 5, Table V) (Control Experiment)

In this experiment 980 cc of a solution containing 0.9 per cent NaCl plus five per cent dextrose were infused intravenously during three hours, as in Experiments 1 and 2. Figure 5 shows the effects of diluting the plasma with 0.9 per cent sodium chloride

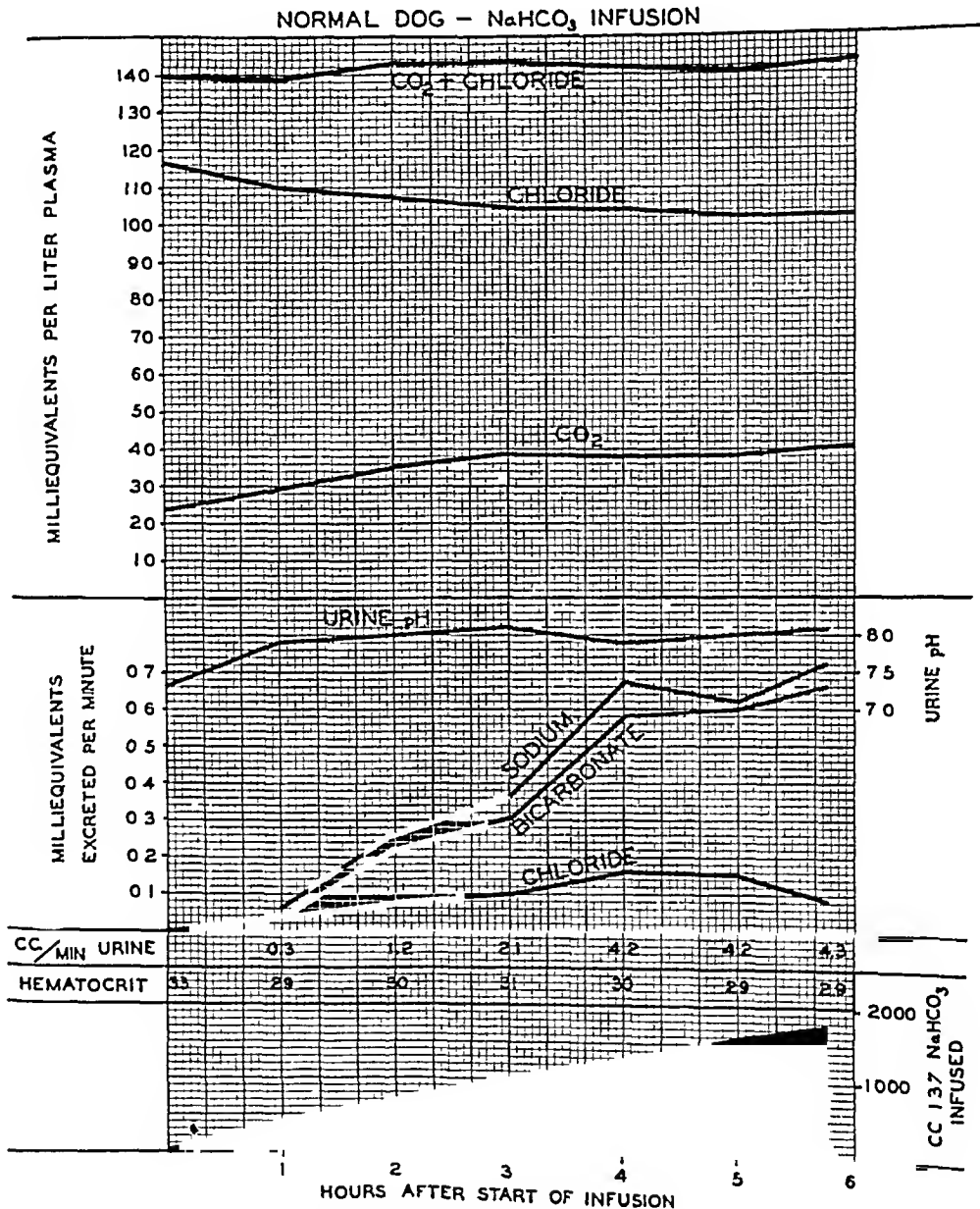


FIG 6—Control experiment showing the effects of 1.3 per cent (isotonic)  $\text{NaHCO}_3$  + 5 per cent dextrose infusion into a normal dog

solution (Cl concentration 154 mEq/L and  $\text{CO}_2$  concentration 0), plasma chloride concentration rose 15 mEq/L and  $\text{CO}_2$  fell from 229 to 17.5 mM/L

Urine chloride concentration, after a peculiar fall in the first period, increased and reached 7.9 Gm/L, with a parallel increase in the rate of chloride excretion. The bicarbonate excretion rapidly fell to zero and remained there while the urine pH fell from 6.5 to 4.6. In this and other similar experiments the kidney bicarbonate threshold was

at about 20 mEq/L Pitts,<sup>20</sup> under somewhat different conditions, found the bicarbonate threshold at about 25 mEq/L

Comparison of this experiment with those of the hypochloremic dog reveals opposite effects on the urine pH. In the initially normal dog the urine pH falls as the plasma bicarbonate is decreased. In the hypochloremic dog, urine pH rises as the increasing plasma sodium chloride content releases the excess plasma sodium bicarbonate for excretion.

#### Experiment 6 The Effect of Infusing 13 Per Cent $\text{NaHCO}_3$ + 5 Per Cent Dextrose Into Normal Dog (Fig 6, Table VI)

This dog received 1000 cc of isotonic sodium bicarbonate solution during the first three hours (compare Experiments 2 to 5) and 770 cc more during the next three hours. The dog, at the start, was apparently somewhat dehydrated, as indicated by the low initial urinary volume and Cl and Na excretion (Fig 6). The first three hours the dog excreted 2.9 Gm of  $\text{NaHCO}_3$ , or 22 per cent of the amount at that time infused. At the end of the six-hour infusion, 10.7 Gm of  $\text{NaHCO}_3$  had been excreted, or 46 per cent of the total 23 Gm infused.

The chief difference in results from those of  $\text{NaHCO}_3$  infusion into the hypochloremic dog of Experiment 3, is that in the normal dog the  $\text{NaHCO}_3$  infusion caused a significant increase in urinary chloride excretion, although less than in bicarbonate output. The hypochloremic dog (Experiment 3) excreted practically no chloride. Only the hypochloremic dog suffered convulsions during bicarbonate infusion.

#### DISCUSSION

The results presented confirm Hartmann<sup>6</sup> and Gamble<sup>2</sup> in showing that *loss of gastric juice produces a condition of dehydration, hypochloremia and alkalosis that is paradoxical in that severe alkalosis (high plasma bicarbonate) is accompanied by excretion of acid urine*. The results also confirm Hartmann and Gamble to the effect that *dehydration, deficit in plasma Cl and Na, and excess of plasma bicarbonate, can be corrected by infusion of isotonic NaCl solution, which also causes the urine to become alkaline*. The initial acidity of the urine does not indicate the desirability of alkali therapy, which would increase the internal alkalosis. The results emphasize the importance of guiding the therapy in this condition by determination of plasma  $\text{CO}_2$  and chloride. Estimations of hematocrits and plasma protein concentration as indicators of dehydration are also valuable, each may be 50 per cent above normal.

The paradoxical low pH of the urine in the face of internal alkalosis is attributable to the almost complete absence of bicarbonate from the urine. The deficit of sodium salts in the body is so great that the kidneys stop excretions of both NaCl and  $\text{NaHCO}_3$ . As shown by Gamble<sup>3</sup> and Sendroy, Seelig and Van Slyke,<sup>4</sup> the urine always contains free  $\text{H}_2\text{CO}_3$  in equal or greater concentration than the blood, so that if no  $\text{NaHCO}_3$  is excreted, the pH will fall to that of a solution of such  $\text{H}_2\text{CO}_3$  concentration, viz, about pH 5.

Infusion of NaCl, by correcting the body's deficit of sodium salts, permits excretion of  $\text{NaHCO}_3$  and rise of urine pH. One encounters another apparent paradox in that infusion of neutral NaCl solution causes excretion of alkaline, bicarbonate-containing urine.

The results of Experiment 1 and 2, with infusion of NaCl into dogs

suffering from dehydration, chloride deficit and alkalosis from loss of gastric fluid also show that

- 1 In severe dehydration from loss of gastric juice, NaCl infusion corrects the abnormalities of the plasma electrolyte pattern by three mechanisms (a) the lost sodium chloride and water are replaced, (b) the excessive bicarbonate concentration in plasma and interstitial fluids is decreased by dilution with the infused chloride solution and (c) plasma bicarbonate is further lowered by excretion of bicarbonate in the urine in large amounts
- 2 To complete the correction of the plasma pattern, large amounts of NaCl solution must be infused. To restore plasma Cl and  $\text{HCO}_3$  to approximately normal concentration, the 20-kg dog in Experiment 1 required 3 liters of 0.9 per cent NaCl solution, or 150 cc per kg, which was infused during the first eight hours
- 3 Reappearance of chloride in the urine could not be used as indication that enough saline had been infused to correct the plasma electrolyte pattern. In Experiment 1, after infusion of 100 cc of 0.9 per cent NaCl per kg, chloride concentration in the urine reached 20 mEq/L (0.71 Gm per liter) when plasma chloride was still only 90 mEq/L (compared with normal dog's 110–120) and plasma bicarbonate was 36 mM/L (normal 20–25). It was only towards the end of the infusion, when chloride concentration in the urine reached about 100 mEq/L (6 Gm NaCl per liter), that plasma values approached normal (Cl 105 mEq/L,  $\text{HCO}_3$  29 mM/L), and they were still not quite back to normal. *When normal plasma electrolyte pattern was approached, the urine Na concentration rose to a level equal to that of the infused fluid (154 mEq/L), and the sum of urinary Cl +  $\text{HCO}_3$  concentration also approximated 154 mEq/L*
- 4 During the large NaCl infusion of Experiment 1, the concentration of cations other than sodium and magnesium (total base concentration—sodium concentration fell from 122 mEq/L to 40 mEq/L). Plasma potassium determinations showed a fall from 3.9 to 2.2 mEq/L. These results suggest when large volumes are infused, that it is advisable to use a balanced infusion solution of  $\text{NaCl} + \text{KCl} + \text{CaCl}_2 + \text{MgCl}_2$  instead of simple NaCl solution

An unexpected point of interest is the apparent difference in the plasma thresholds for excretion of chloride and sodium in dogs that are passing from normal hydration to dehydration, compared with dogs that are passing in the opposite direction, from the dehydration (caused by loss of gastric juice) to normal hydration by saline therapy. In the normal dogs, we have seen a 24-hour fasting period cause almost complete suppression of Na and Cl excretion, although the plasma Cl was still at the normal level of 110–115 mEq/L, and  $\text{Cl} + \text{HCO}_3$  at 140. When hypochloremic dehydrated dogs were infused with NaCl, however, chloride excretion started by the time the plasma chloride had reached 80 mEq/L, and plasma  $\text{Cl} + \text{HCO}_3$  was not over 120 mEq/L (Experiment 1). The kidneys in the salt depleted dogs had apparently lowered their chloride threshold and, when the chloride depletion was in process of correction by saline infusion, the kidneys began to excrete salt much before the normal plasma level was regained. A diagnostic corollary appears

to be, that when a condition of salt depletion is being established, drop of chloride excretion to a low rate is a more sensitive indicator of the condition than is the plasma chloride concentration. But when the condition of depletion of the type caused by loss of gastric juice is in process of correction by NaCl administration, restoration of normal plasma chloride concentration shows more accurately than resumption of chloride excretion when enough saline has been given to correct the condition.

#### SUMMARY

The condition of dehydration, hypochloremia and alkalosis, observed after severe loss of gastric juice by vomiting or gastric suction, has been reproduced in dogs by the total gastric pouch method of Dragstedt and by gastrostomy with pyloric ligation.

Despite the alkalosis (excess plasma bicarbonate) the urine was acid (pH 5 to 6.4). The acidity of the urine is attributed to the fact that the body deficiency of sodium salts is so great that excretion of both NaCl and NaHCO<sub>3</sub> is almost completely stopped, in the apparent effort to preserve what is left of the body's store of sodium salts. In the absence of bicarbonate in the urine, the pH falls towards that of a solution of free H<sub>2</sub>CO<sub>3</sub>.

Sodium chloride infusions corrected the alkalosis and dehydration, replaced the lost plasma sodium and chloride, and permitted excretion of the excess NaHCO<sub>3</sub>, which raised the urine pH to 7.5-8.0.

During saline infusion resumption of chloride excretion was not a safe sign of adequate replacement, replacement was adequate only when plasma chloride concentration was restored to a normal level.

Massive infusion of a solution of NaCl plus glucose was observed to decrease the plasma potassium to less than half the normal concentration, and, by indirect estimation, also the calcium. These effects indicate the desirability of using a balanced electrolyte solution of Na, K, Ca, and Mg when large infusions are given.

Sodium bicarbonate infusion did not correct the plasma electrolyte pattern, raised urinary pH above the physiologic range (pH 8), and caused tetanic convulsions.

The results indicate the possible dangers of using sodium bicarbonate to alkalinize the urine of patients suffering gastric fluid loss, the advisability of using NaCl infusions, and the desirability of guiding the therapy by plasma analyses including at least chloride and CO<sub>2</sub> determinations.

We wish to express our appreciation to Dr. Ole Malm and to Dr. Howard Eder for determining the plasma total base, sodium, and potassium concentration in experiments 1 and 3, and to Dr. D. D. Van Slyke for his great help in analyzing and discussing the data presented.

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# ESSENTIAL THERAPEUTIC ADJUVANTS IN THE SURGICAL ARREST OF WOLFF-ISRAEL ACTINOMYCOSIS\*†

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THE CLINICAL MANAGEMENT of extensive actinomycotic infections has been considerably advanced by potent antibacterial therapy and an improved understanding of the metabolic requirements of the depleted patient<sup>1</sup>. Therapy with sulfonamides or penicillin has largely replaced treatment with X-ray and such drugs as iodides or thymol. Attention has been directed to a high dietary intake of protein and calories. Even so, it has become increasingly apparent that no form of therapy can substitute for the surgical drainage of pus or excision of tissue devitalized by infection. As attempts at surgical eradication of the disease have become more radical, we have been impressed with the poor tolerance for blood loss and surgical trauma encountered in these chronically ill patients. Further, wound healing has been delayed or faulty, convalescence has been prolonged and some patients have shown incomplete arrest of the disease.

The depletion of reservoirs of body protein seen so frequently in patients with chronic infection is especially common in the patient with advanced Wolff-Israel actinomycosis. Profound anemia and significant weight loss are clinical features of the disease with visceral involvement. Several such patients presented themselves for treatment during a period when we were engaged in a study of the hemoglobin deficiency in chronic shock and the problems of reduced blood volume in the chronically ill patient. Observations of the quantity of blood necessary to overcome the anemia in patients with actinomycosis revealed an unexpectedly great deficit in the total circulating mass of red blood cells. The improved tolerance for surgical blood loss and the acceleration of wound healing noted after blood volume restoration were especially striking. Weight gain and convalescence were rapid in those patients with an adequate dietary intake.

## CLINICAL OBSERVATIONS

Five bacteriologically proven cases of Wolff-Israel actinomycosis provide the source material for this discussion. All presented extensive involvement persistent over a considerable period of time. The essential clinical data are summarized in Table I. Although seriously ill, no patient required emergency measures at the time of admission. There was ample opportunity for thorough study and evaluation of the patient anticipatory to election of a surgical program of treatment.

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† This is publication No. 5 from researches accomplished under a grant from the Office of the Surgeon General, United States Army.

Secondary anemia and deficiency of body weight were characteristic features of this chronic disease. The deficit in hemoglobin was frequently more apparent on clinical examination than from laboratory estimations of the hemoglobin concentration or hematocrit percentage. The quantity of blood necessary to restore the hematocrit to the range of normal was also in excess of that predictable on the basis of the initial hemotocrit value. The deficiency in body weight was made especially prominent by the increase recorded during convalescence. (See Table II)

TABLE I

SUMMARY OF PERTINENT CLINICAL DATA IN FIVE CASES OF PROVEN WOLFF-ISRAEL ACTINOMYCOSIS. ALL RECEIVED BLOOD TRANSFUSIONS. CHEMOTHERAPY WITH PENICILLIN AND HIGH PROTEIN-HIGH CALORIC DIET

Patient	Race	Sex	Age	Site	Duration	Surgery	Result
1 G H	W	F	20	Cervico-fascial	2½ yrs	0	Arrested
2 G T	W	F	45	Pleuro pulmonary-mammary	1½ yrs	+	Arrested
3 M M	W	M	34	Pleuro-pulmonary-cutaneous	6 mos	+	Arrested
4 E W	C	M	43	Abdomino-cutaneous	10 mos	0	Recurred 13 mos
5 O P	W	M	73	Mandibulo-facial	8 mos	+	Arrested

TABLE II

COMPOSITE TABLE OF INITIAL AND FINAL HEMATOCRIT VALUES IN RELATION TO TOTAL QUANTITY OF BLOOD GIVEN AS TRANSFUSIONS. ALL PATIENTS ABLE TO EAT SHOWED SIGNIFICANT GAIN IN BODY WEIGHT

Patient	Initial Hematocrit	Blood Given	Final Hematocrit	Weight Gain
1 G H	34	3500 cc	44	24 kilos
2 G T	34	7000 cc	38	7 kilos
3 M M	36	2000 cc	50	9 kilos
4 E W	28	3500 cc	40	18 kilos
5 O P	26	3500 cc	46	-9 kilos*

\* Patient O P was temporarily unable to eat following resection of one ramus of the mandible

The true deficiency of circulating red blood cells was more accurately revealed by blood volume determinations than by any other available method. These measurements were performed by the plasma-dye-hematocrit method and standard values were calculated on the basis of the patient's usual weight in health. The results confirmed the existence of "chronic shock," the reduced blood volume associated with weight loss (Lyons *et al*)<sup>2</sup>. The characteristic findings in our cases are illustrated in the record of patient No. 2 (G T) as presented in Table III. It is significant that the transfusion of 7,000 cc of whole blood during the period of hospitalization failed to provide total correction of the estimated deficiency at any time.

In the clinical management of these patients we have been especially interested in four features of the response to therapy: correction of anemia, tolerance for surgical blood loss, wound healing and gain in body weight. With the one exception noted below, all patients were able to accept and retain a high caloric, high protein diet.



*Patient No 1* (G H, O C No 19053) had been continuously ill for two and one-half years. Recurrent and persistent sinuses in the postero-lateral portions of the neck were communicant with an abscess of the prevertebral

TABLE III  
Patient No 2 G T

SUMMARY OF BLOOD VOLUME CHANGES DURING PERIOD OF SURGICAL MANAGEMENT AND CONVALESCENCE. A TOTAL OF 7000 CC OF BLOOD WAS GIVEN FROM MAY 2-JUNE 22 WITHOUT EVIDENCE OF OVERLOADING THE VASCULAR RESERVOIR

Date	Remarks	Total Cell Mass	Blood Volume	Body Weight
May 2	On admission	1500 cc	4100 cc	71.7 kilos
May 7	After 2000 cc blood and thoracotomy	2400 cc	4900 cc	70.8 kilos
May 20	After acute sulfadiazine anemia and 2500 cc blood	2100 cc	4600 cc	69.4 kilos
June 22	After two more operations and 2500 cc blood. Healed	2200 cc	5500 cc	70.3 kilos
July 20	One month after discharge	2000 cc	5100 cc	72.6 kilos
Nov 5	Working	1900 cc	5000 cc	78.5 kilos
	Standard for usual weight of 72.7 kilos	2900 cc	6100 cc	

### Actinomycosis of Prevertebral Fascial Plane with Cervical Sinuses

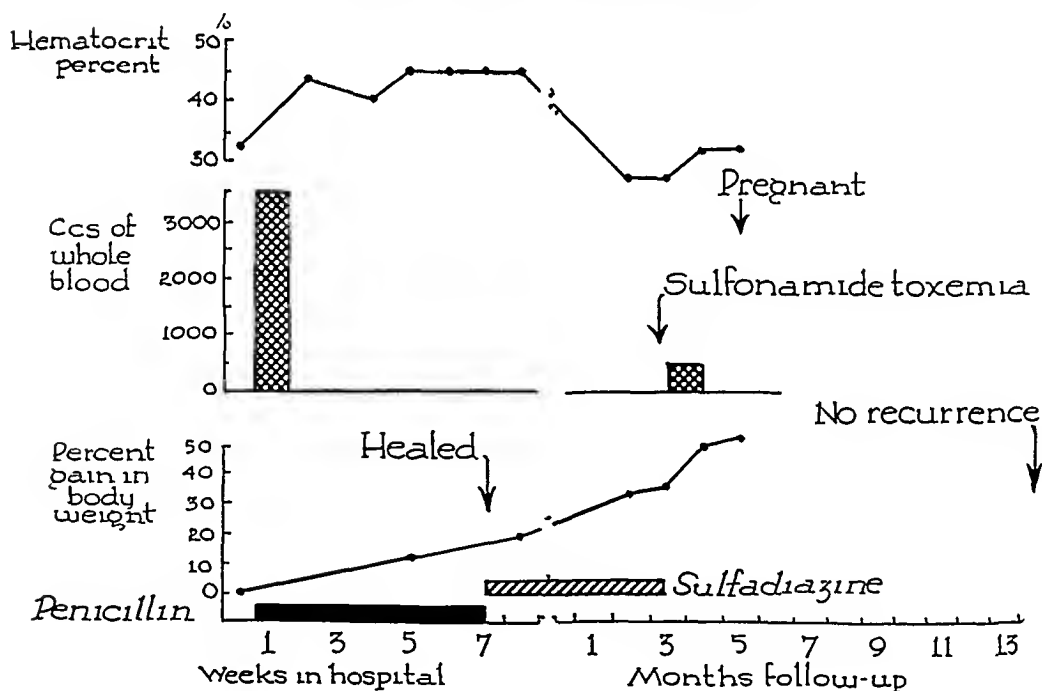


FIG 1

fascial plane. Destruction of the anterior surfaces of the vertebral bodies was noted on X-ray. Repeated periods of hospitalization for penicillin therapy had failed to arrest the disease and prolonged sulfonamide therapy had been

similarly ineffectual. This same program of therapy was reinstituted after transfusion of 3,500 cc of whole blood and restoration of the total circulating cell mass to standard value. Wound healing and gain in body weight were noted promptly as shown in Figure 1. It has seemed reasonable to conclude that the therapeutic correction of blood protein deficits by transfusion of whole blood was a measure of critical importance in this patient.

*Patient No 2* (G T, O C No 46009) developed pulmonary actinomycosis one and one-half years prior to study. Chest wall and mammary extension were later features of the disease. At the time of admission to the hospital

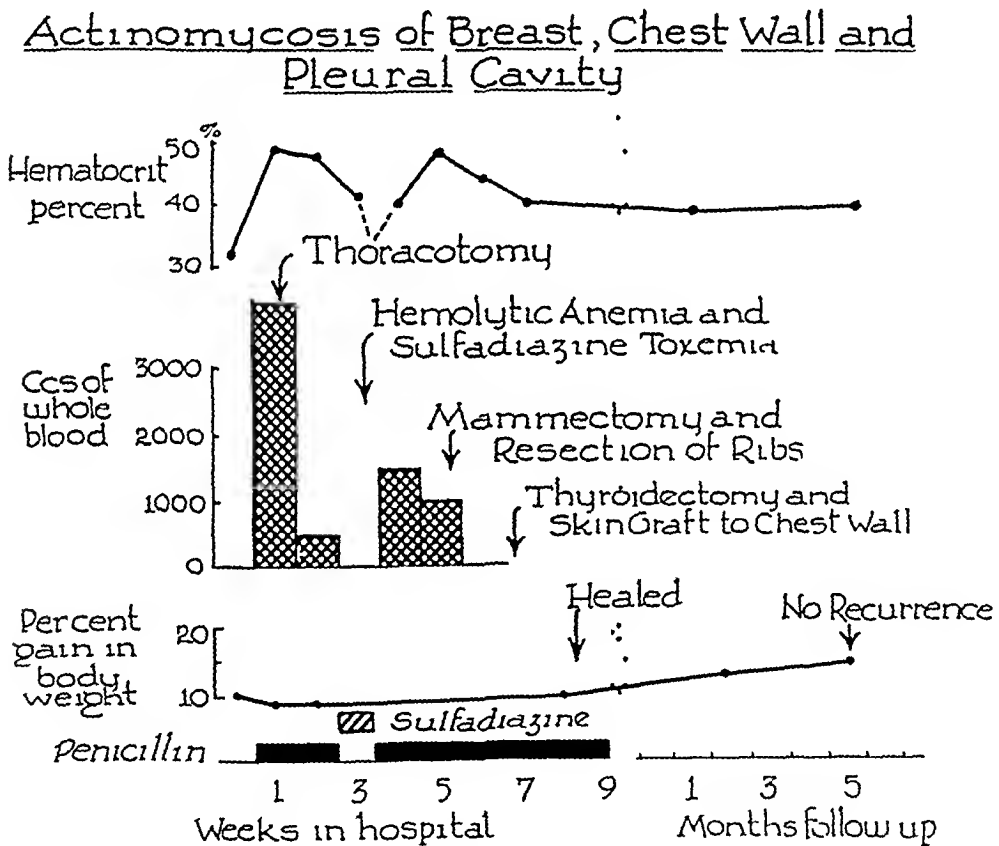


FIG 2

there were multiple sinuses and a major empyema. Extensive surgical procedures were necessary in stages to provide (1) drainage of pus, (2) excision of tissue devitalized by infection, and (3) skin coverage of chest wall defects. The blood loss incident to these operations was considerable. As has been noted in Table III, complete replacement of the total circulating red blood cell mass was never achieved. The tolerance for surgical blood loss and the rapidity of wound healing were clinically satisfactory (See Chart II). However, weight gain was a delayed feature noted in later convalescence.

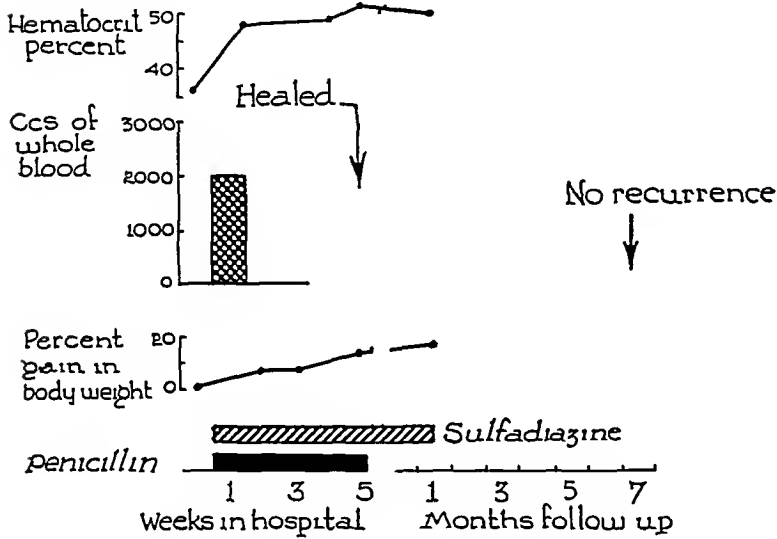
Pleuro-Pulmonary-Cutaneous Actinomycosis

FIG 3

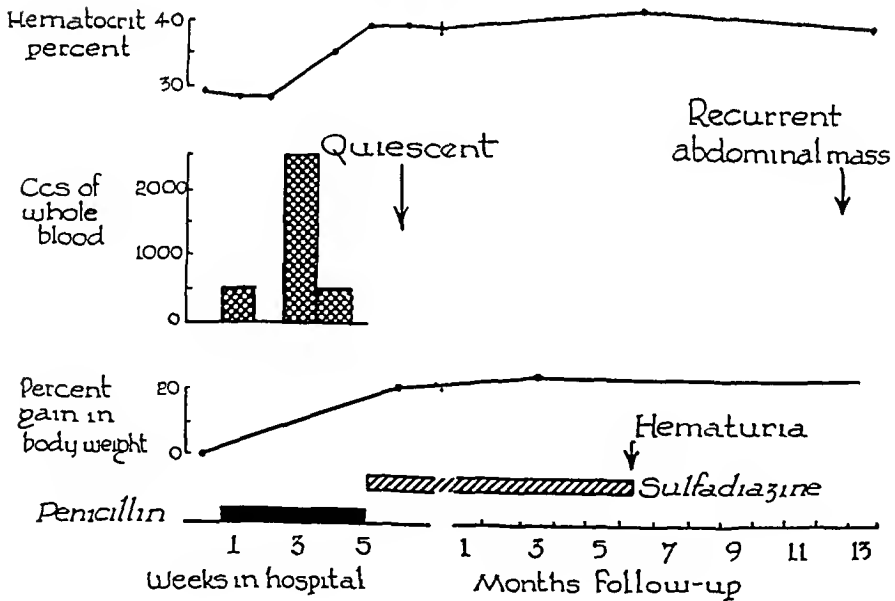
Abdominal Actinomycosis

FIG 4

*Patient No 3* (M M, O C No 44978) was referred for diagnosis and treatment of bilateral pleural and pericardial effusions of six months' duration. Shortly after admission an inflammatory mass appeared in the anterior axillary line in the eighth interspace. Incision of this tumefaction established the presence of Wolff-Israel organisms. Shortly thereafter, a similar swelling appeared on the opposite chest wall. Effective therapy consisted of pleural aspirations, transfusion correction of the anemia, penicillin therapy and high protein diet (See Figure 3).

*Patient No 4* (E W, C H No T-45-172215) was admitted in May, 1945, for treatment of an abdominal mass and fistula in the right lower quadrant following drainage of an abscess. Rectal fistulas were also present. For a period of seven months he received sulfonamide or penicillin therapy nearly continuously with only moderate improvement. In November, 1945, he was readmitted with recurrent pain and fever. The only new therapeutic procedure introduced at this time was the correction of anemia by transfusion of 3,000 cc of blood. Within one month, the patient was healed and free of symptoms for the first time (See Fig 4). The recurrence noted after 13 months' arrest of the disease suggests to us that surgical excision of the lesion should have been done during the period of maximum recovery.

*Patient No 5* (O P, O C. No 42873) was admitted with classical actinomycosis of the face with involvement of the mandible. Correction of anemia by transfusion restoration of the blood volume enabled this frail and elderly (aged 73 years) man to undergo the necessarily extensive excision of diseased tissue with resection of the mandible. Postoperatively an adequate oral intake was temporarily impossible and weight loss was noted. Wound healing, however, was uneventful.

The general efficacy of the program of management adopted is apparent from Table IV. In all of these seriously ill patients, wound healing and significant arrest of the disease were accomplished within four to seven weeks of hospitalization.

It is apparent in Figures 1-5 that penicillin has been adopted as the antibacterial agent of choice during the period of hospital management. In adequate dosage of 25,000-50,000 units every two to three hours, it has proven fully effective against the actinomycetes and relatively free of toxic reactions. Sulfonamides have been reserved for prolonged therapy in patients with surgically inaccessible disease after convalescence has become established. Rejection of sulfonamides as the chemotherapeutic agent of choice for initial therapy has been necessitated by many considerations. The incidence of toxic or urinary tract complications attributable to sulfonamides has made them undesirable during a period of complicated surgical management. Further, these drugs are contraindicated in depleted persons because of the known depressant effect upon hematopoiesis, the intestinal synthesis of essential metabolites, and the appetite in general. Even when used during established convalescence, the sulfonamides are frequently impractical (See Table V).

## DISCUSSION

At the present time, the management of serious actinomycotic infections has emphasized (1) antibacterial therapy, (2) high dietary intake of protein with adequate calories, and (3) drainage of pus and surgical excision of tissue devitalized by infection. As an essential feature of this program, we wish to add transfusion of whole blood in quantities sufficient to restore the total circulating red blood cell mass to or slightly below the standard for the patient's standard or usual weight in health.

TABLE IV

TABLE SHOWING PERIOD OF HOSPITALIZATION NECESSARY FOR CLINICAL ARREST OF THE DISEASE AND WOUND HEALING

Patient	Pre Operative Hospital Stay	Number of Operations	Total Hospital Stay
1 G H		0	42 days
2 G T	5 days	3	46 days
3 M M		1	27 days
4 E W		0	49 days
5 O P	8 days	1	31 days

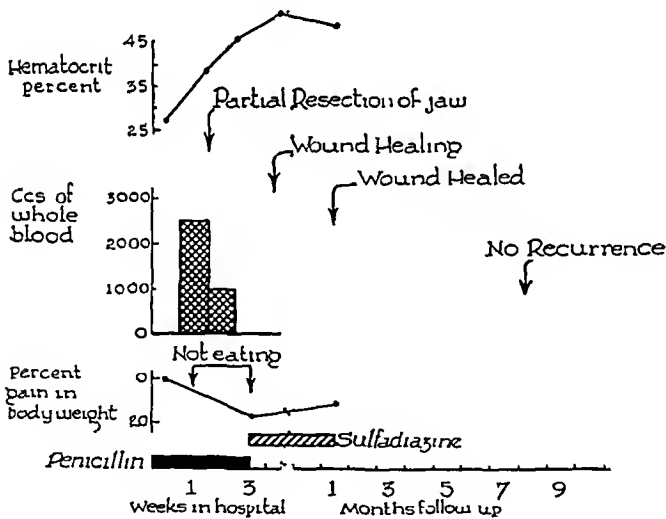
Mandibulo-Facial Actinomycosis

FIG 5

Most surgeons will concede considerable blood loss in the excision of the inflammatory mass typically associated with Wolff-Israel actinomycosis. We have become especially aware of this factor and believe that transfusions of whole blood before and during surgical operations provide the only available method of improving tolerance for surgical blood loss.

Anemia is a prominent feature of actinomycotic infections. A fundamental defect in hemoglobin metabolism in patients with chronic infections has been elucidated by Wintrobe *et al*.<sup>3</sup> Whipple and his co-workers<sup>4</sup> have emphasized

the prior demand of needed hemoglobin upon newly available dietary protein. These basic facts suggest that antibacterial therapy, transfusion of blood and drainage of pus constitute initial therapy in chronic infections.

Within Schoenheimer's<sup>5</sup> concept of "dynamic equilibrium," Whipple and associates<sup>6</sup> have elaborated the thesis of a "metabolic pool" of "labile protein reserves." The chief reserves of protein are in the tissue cells. In simple malnutrition with anemia, the demand for blood proteins will further deplete the already diminished reserves of tissue protein unless the dietary intake of food protein be abundant.<sup>7</sup> In chronic sepsis with nutritional depletion and anemia, this phase of protein metabolism is complicated by the inability to produce new

TABLE V

SUMMARY OF DRUG THERAPY AS ADMINISTERED DURING AND AFTER HOSPITALIZATION IN THREE OF THE FIVE PATIENTS. A TOXIC REACTION WAS NOTED IN CONSEQUENCE OF SULFONAMIDE THERAPY. A MILD ANEMIA WAS CHARACTERISTIC OF PROLONGED SULFONAMIDE THERAPY.

Patient	Days of Penicillin Therapy	Days of Sulfadiazine Therapy	Sulfonamide Toxemia
1 G H	39 days	96 days	+
2 G T	42 days	4 days	+
3 M M	14 days	27 days	0
4 E W	36 days	169 days	+
5 O P	20 days	82 days	0

hemoglobin and new red blood cells. The only satisfactory method of correcting the anemia in chronic infections is the transfusion of whole blood in amounts adequate to restore the total circulating red blood cell mass to standard values. This permits utilization of protein reserves primarily for wound healing.

Our observations suggest that after correction of anemia the wounds heal even though tissue protein reserves are not replaced immediately. Adequate wound healing has been noted in patients without concomitant weight gain. Apparently, the synthesis of new protein assigns priority to wound healing rather than to replenishment of tissue protein reservoirs. Restoration of tissue protein depends upon the intake of food protein and calories in excess of normal requirements. The most important and reliable evidence of this replacement is progressive and sustained weight gain. Thus, blood transfusion and adequate protein intake are both essential features of the supportive nutritional program in the surgical arrest of the disease.

#### CONCLUSIONS

- 1 Depletion of blood proteins is a significant feature of the malnutrition observed in patients with Wolff-Israel actinomycosis.
- 2 Precise evaluation of the anemia and hypoproteinemia demands repeated blood volume determinations throughout the period of clinical management.
- 3 Transfusion of whole blood in quantity sufficient to restore the total

circulating red blood cell mass is obligatory in the pre-operative preparation of the patient

4 Replacement of blood lost during surgical operations demands whole blood transfusions to maintain the pre-operative status

5 Postoperatively, maintenance of the blood proteins is necessary to divert labile protein reserves to the purposes of wound healing

6 Replenishment of tissue protein reserves, as evidenced by weight gain, demands an intake of food proteins and calories in excess of normal requirements

7 Penicillin is the antibacterial agent of choice during the period of hospitalization and initial surgical management Sulfonamides (sulfadiazine) are reserved for prolonged medication during convalescence

8 The surgical procedures recommended in the treatment of actinomycosis are

- (a) Drainage of abscesses
- (b) Excision of accessible foci of devitalized and infected tissue
- (c) Reparative closure of resultant tissue defects by secondary suture, sliding or pedicle flaps and free skin grafts

9 Under this program of management the disease has been promptly arrested, wounds have healed and body weight has been restored

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DISCUSSION—DR RUDOLPH MATAS, New Orleans I want to congratulate Doctor Gage and Associates on their success in improving the prognosis of actinomycosis The results of chemo-therapy with the sulfonamides is disappointing as must be expected in resorting to drugs so unfit for prolonged administration, especially in the chronic visceral lesions that are so inaccessible to surgery The combination of penicillin with massive whole blood transfusion and high dietary intake of protein, is a decidedly valuable contribu-

tion in which the advances in therapeutic hematology may justly claim even a greater share of credit for the result than surgery with or without the aid of antibiotics. The old recognized value of potassium iodide should not be overlooked in the excitement of the new therapy.

DR ALTON OCHSNER, New Orleans. Doctor Gage's presentation is more significant than would appear at first thought, not only because of the results he has obtained in the treatment of actinomycosis, a disease which in its extensive form has defied treatment, but also because of the results obtained in other chronically ill patients. Dr. Champ Lyons for the past two years has been carrying on extensive investigations on our service at Tulane and has found that the chronically ill patients suffering from chronic infection, specific and non-specific, and suffering from neoplasms have alterations in their blood volume which are not detected by the ordinary laboratory examination. Although many of these patients appear to have no anemia because of the relatively normal hemoglobin per cent value and relatively normal red cell per cu mm value, they actually have severe anemia because of a contracted blood volume. One must know the total circulating hemoglobin and the total circulating red cell mass to treat these chronically ill patients satisfactorily. This can be ascertained only by the determination of the blood volume.

Dr. George Whipple has shown that there is a preferential demand on protein for the synthesis of hemoglobin, and in the individual who has a deficient amount of hemoglobin, the protein taken in may be utilized entirely for the synthesis of hemoglobin and may not be available for repair of tissues. This is particularly important in the chronically ill patient, such as the one with actinomycosis.

For some time we have known empirically that the chronically ill patient required blood preoperatively, because we knew that unless they received blood before operation, they could not withstand a major surgical procedure without getting into difficulty. Without knowing what their actual deficiency was, we were at a loss to know what to give them. By the determination of the blood volume we can estimate what their actual deficiency is and correct this by the administration of adequate amounts of whole blood. During the past two years we have found that in our chest patients an average of 2.5 liters of blood was required preoperatively to replenish their deficiency.

The anemia associated with actinomycosis is especially important because if sulfonamides are used therapeutically the anemia is likely to be aggravated. It is because of this, as emphasized by Doctor Gage, that the chemotherapeutic management early in the course of the disease should consist of the administration of penicillin rather than sulfonamides. Later, after the anemia has been corrected and after repair of the tissue has begun, sulfonamides can be started and must be continued for a long period of time, usually for many months. With the institution of the regimen outlined by Doctor Gage and his associates, we have been able to control and to bring about a cure in cases of actinomycosis which previously would not respond to any type of therapy. Although my remarks have been concerned principally with the anemias and chemotherapy, I would not want to leave the impression that surgical therapy is not equally as important in these cases.

DR I. S. RAVDIN, Philadelphia. Doctor Gage is to be congratulated on this presentation. In his paper yesterday, Doctor Zintel pointed out a similar mechanism in the treatment of patients with carcinoma of the colon. It has universal application in patients who have a hemoglobin deficiency, and at the same time a deficiency in the reserve stores of protein. Regardless of the type of feeding, the protein and minerals will go to restoring hemoglobin, and not toward replenishment of the protein stores. I think attention should be called to the work of Paul Cannon on the control of infection under such circumstances. He has pointed out that as soon as a protein deficiency exists in the experimental animal, antibody formation and phagocyte formation is retarded. Thus, two of the biologic factors which have to do with control of infection are disturbed.

In speaking of diet under the circumstances described by Doctor Gage, one should



remember that though it is important to give adequate protein, if large amounts of carbohydrate and protein are fed, the fat content of the diet can be increased, then you can prevent large losses of protein in the urine. Where liver protection is not so important, the restriction of fat is not so important.

DR MIMS GAGE, New Orleans (closing) In answer to Doctor Churchill's question, I would state that we use the plasma dye technic to determine the blood volume. The technic may be criticized as to its accuracy. However, we believe that it is sufficiently accurate to demonstrate and call our attention to the presence of chronic shock in the chronically ill or debilitated patient. By the use of plasma dye method in estimating the blood volume preoperatively, we have been able to demonstrate the presence of chronic shock, overcome this state of chronic shock, return the patient to a normal physiologic basal line, making it possible to proceed with major surgical procedures with most gratifying postoperative convalescent and clinical curves. I am convinced that by determining the blood volume in the chronically ill patient and restoring the patient to physiologic balance we have saved many lives which would have been lost without the above knowledge.

# AN EVALUATION OF METHODS OF PENICILLIN THERAPY IN THORACIC SURGERY\*†

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PENICILLIN is now being widely used in the active treatment of or prevention of infection in many medical and surgical conditions. Various methods of administration have been recommended and are now being used, whereas the final decision as to which are best or preferable have not been made. The ideal method may vary according to the condition under treatment. It was thought worthwhile to determine concentrations of penicillin in blood serum and pleural fluid following technics of administration commonly employed, and to consider their relative merits. This study was made on humans and on dogs having intrathoracic operations in which a lung lobe or an entire lung was resected.

It is believed by the authors that the study of penicillin titers in appropriate body fluids affords a somewhat more controlled means of evaluating relative therapeutic efficacy of a given method of administration than is possible by clinical observation in a comparable number of patients. Without large numbers of patients, affording statistical proof of the superiority of a given technic by its therapeutic response, clinical observation may be misleading.

*In Vitro* studies by Rammelkamp and Keefer<sup>1</sup> indicate that penicillin has a bactericidal effect on hemolytic streptococci in serum in concentrations of as little as 0.015 Florey units per cc. They state that a concentration between 0.03 and 0.3 units per cc. of whole blood was necessary for maximal killing of the hemolytic streptococcus.

*Staphylococcus aureus* was found in general to be more resistant to the drug, requiring about 0.15 units per cc. of penicillin for maximum killing effect. Growth of organisms is inhibited at considerably lower concentration. They noted that as the blood titer of penicillin falls following intramuscular administration, the bactericidal action tends to be maintained, and that there was an anti-staphylococcic action of the whole blood for almost an hour after the serum concentration of penicillin was too low to detect.

Different strains of staphylococci exhibit wide variations of susceptibility to penicillin, sensitivity ranging from 0.02 units per cc. to 0.35 units per cc. for bactericidal effect of 29 strains tested in veal infusion broth.

Other organisms display a wide range of susceptibility to penicillin, and dosage and technic of administration should be regulated accordingly.<sup>2</sup>

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\* Read before the American Surgical Association, March 26, 1947, Hot Springs, Va.

† This work was done in part under a grant from the Etta Baker Fund for Tuberculosis Research.

## METHODS

Intramuscular, intratracheal, aerosol, and intrapleural administrations of penicillin were studied with assays made on serum, and in some instances pleural fluid, at given time intervals following administration. Most of the determinations were made from clinical material. Studies on dogs, most of which had undergone pneumonectomy for other experimental purposes, were used to supplement clinical data. A tabulation of the number of experiments performed appears in Table I. In general each experiment represents a single administration of penicillin followed by one to several fluid level determinations made at various intervals.

TABLE I  
PENICILLIN THERAPY

Method of Administration	Experiments Performed			
	Man		Dog	
	Serum	Pleural Fluid	Serum	Pleural Fluid
Intramuscular	16	20	4	0
Intratracheal	9	0	8	0
Aerosol	12	0	10	0
Intrapleural	8	20	12	12
	—	—	—	—
Total	85		46	

Number of experiments performed on patients and on dogs for each of the techniques of penicillin administration studied

Assays were made by a modified cup-agar technic as described by Abraham, *et al*<sup>3</sup> and by Foster and Woodruff.<sup>4</sup> A sensitive strain of *Staphylococcus aureus* was used as the test organism. In general, assay values were considered reliable for penicillin concentrations within therapeutic range, i.e., 0.03 units per cc. and higher.

## RESULTS

## A Intramuscular Injections

*Serum levels.* Serum titers of penicillin following intramuscular injection of 20,000 units are represented in Chart 1. Maximum, average and minimum levels are indicated. Averages, represented by solid lines, are made from four to eight assay determinations for each time interval indicated. It is seen that maximum levels are attained in 15 to 30 minutes after injection. In two hours there is a minimal therapeutic level. This is in general agreement with other investigators in this field<sup>5, 6, 7</sup> (Results of animal experiment agree with humans).

Dogs given intramuscular penicillin, in doses proportional to weight corresponding to 20,000 units for a 70 kg. man, showed a similarly shaped serum-level curve for the first one-and-one-half hours, with maximum levels at one-half hour ranging from 0.34 units per cc. to 0.43 units per cc. At the end of one-and-one-half hours, titers ranged from 0.14 unit per cc. to 0.23 unit per cc.

*Pleural fluid levels* Pleural fluid penicillin levels obtained following intramuscular administration were extremely variable, depending apparently upon the duration of treatment, manner in which the fluid was obtained, i e whether by direct thoracentesis or from a Pezzer catheter or other drainage tube, and perhaps other factors such as the amount of fluid present in the pleural cavity, the presence of infection with penicillinase-forming organisms, and perhaps the condition of the pleural serosa Table II represents values obtained which are thought to be relatively comparable in the conditions under which they were obtained, i e absence of supplementary medication, absence of infection and samples freshly drawn from the pleural cavity

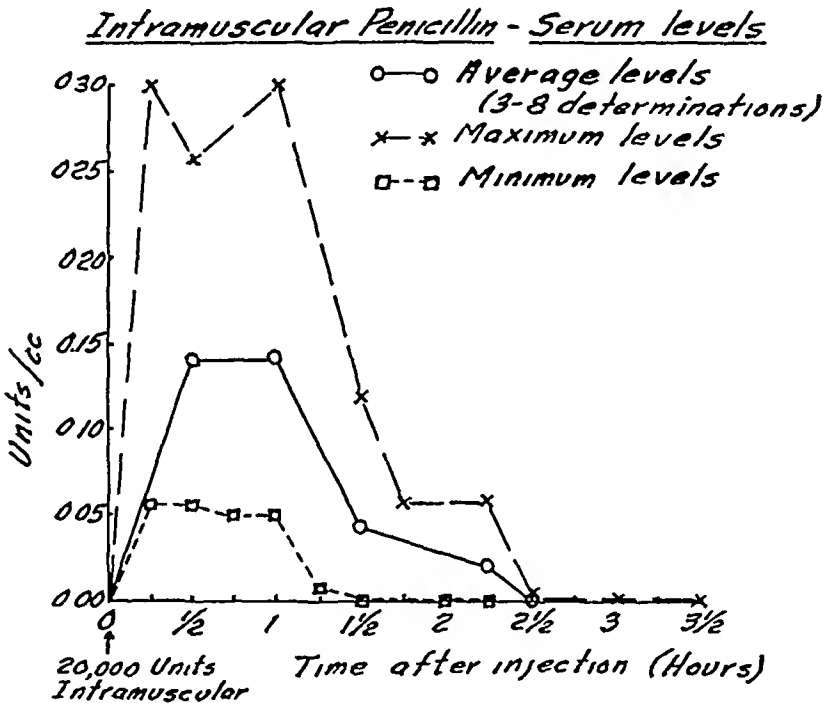


CHART I —Serum levels (units per cc) at various time intervals following intramuscular injection of 20,000 units of penicillin

Pleural fluid penicillin levels are seen to be maintained at therapeutic levels for two hours or longer, reaching a maximum at about one-and-one-half hours after injection On one occasion a penicillin titer of 0.03 units per cc was noted six hours after the last intramuscular injection of 20,000 units

In general it is noted that 40,000 unit doses intramuscularly give more than double the pleural fluid penicillin level rendered by 20,000 unit doses

Cooke and Goldring<sup>7</sup> concluded that the concentration of penicillin in edema, ascitic and pleural fluids tend to approximate that of the blood serum The present study seems to indicate that titers of pleural fluid do not necessarily approximate those of the serum for any particular time after administration but rather fluctuate more gradually and may approximate the median blood serum level over an extended period It would seem that a large amount

of pleural fluid or thickened pleura would cause more gradual fluctuations in the pleural fluid penicillin level

### B Intratracheal Instillations

Intratracheal instillations of penicillin were made on nine patients, usually following bronchoscopy, but on three occasions by use of a Jackson cannula. Results by the two techniques were essentially similar, and are combined in their graphic representation in Chart 2

TABLE II  
PENICILLIN THERAPY

Dose	Hours After Administration			
	$\frac{1}{2}$	1	$1\frac{1}{2}$	2
1 M	u/cc	u/cc	u/cc	u/cc
40 000 U		0.23	0.24	0.15
40 000 U		.27		
40 000 U	0.06	.18	.28	.28
40 000 U	.15			
20 000 U	.24			
20 000 U		.03		
20 000 U	tr			
20 000 U			.12	
20 000 U				.08

Pleural fluid penicillin levels (units per cc) at various time intervals following intramuscular injection of 40 000 U and 20 000 U doses in man

Single experiments were performed with 200,000, 100,000 and 90,000 unit doses (20,000 units per cc in each case). Maximum, minimum and average levels are noted for 50,000 unit doses, average values representing from three to five determinations each.

Maximum levels were uniformly noted after one-half hour, with generally good therapeutic serum penicillin concentrations at that time. By the end of two hours after 50,000 unit doses, minimum therapeutic serum levels were noted, and at three and four hours only traces of the drug were found in the serum. Increased dosage gave correspondingly higher serum levels. The sodium salt was used in these experiments, although calcium penicillin is reported to be more pleasant to take and has less local tissue toxicity<sup>8, 9</sup>

Intratracheal penicillin administered by bronchoscope to eight dogs in doses of 20,000 units (equivalent by weight to approximately 100,000 units in the human) yielded average serum penicillin levels

### C Aerosol Administration

Considerable technical difficulty was encountered in administering penicillin by aerosol efficiently enough to yield detectable blood levels. Use of a BLB mask through which the nebulized penicillin was inhaled resulted in great loss

of the drug due to precipitation of particles on the lining of the mask, apparently because of turbulence of flow consequent to poor streamlining. The best results in blood levels, and presumably also in dissemination of the aerosol throughout the lungs, were obtained as follows. The nebulizer\* outlet is held in the mouth, the lips forming a seal. An oxygen (or compressed air) flow of four to five liters per minute is used. A Y-tube between the oxygen source and the nebulizer has one arm open, acting as an exhaust when the nebulizer is not being actuated. Pressing the thumb over this exhaust opening forces the oxygen through the nebulizer.<sup>8</sup> The patient is instructed to breathe as

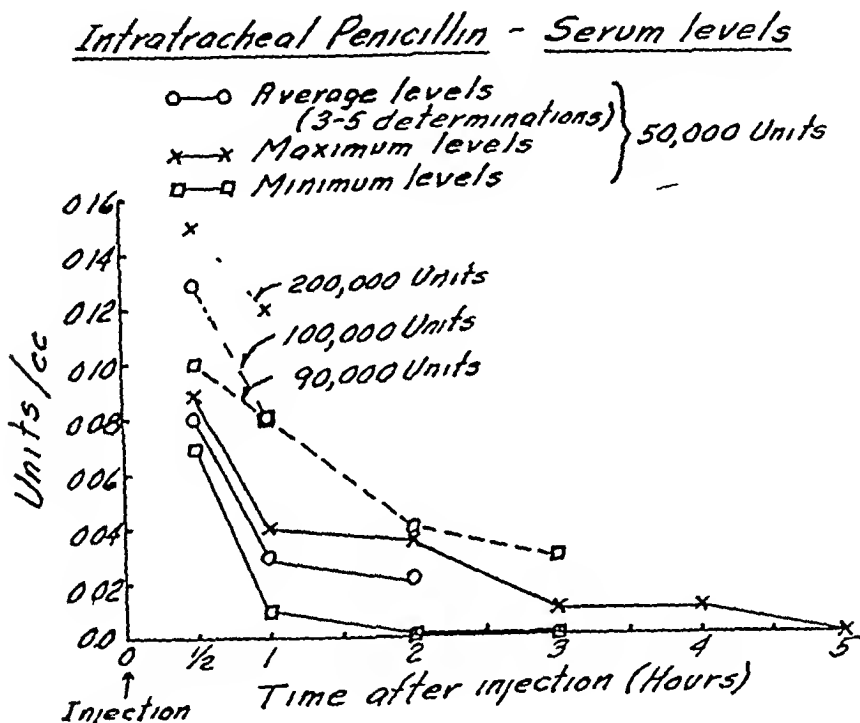


CHART 2—Serum levels (units per cc) at various time intervals following intratracheal administration of penicillin in various doses by bronchoscope or Jackson cannula. (Traces of penicillin are indicated on the graph as 0.01 unit per cc.)

slowly and deeply as is comfortable. During the first half of the inhalation phase the nebulizer is actuated by pressing the thumb over the open arm of the Y-tube, and the patient breathes in through his mouth. The inhalation is completed through the nose with the thumb removed from the exhaust outlet. Expiration is through the nose. A co-operative patient can learn the technic quickly. With ordinary breathing aerosol mists can be seen to be exhaled. Using the technic described, no such mists are visible. Barach, *et al*<sup>2</sup> advocate holding the breath for a moment after inhalation to insure maximum effectiveness. This seems to be less comfortable over an extended period of time than the technique herein described. One or two rinses with one-half to one cubic

\* Made by the Vaponephrin Company. The medium mass diameter of the droplets was approximately 2.5 micron.

centimeter of water or saline in the nebulizer carburator are necessary to deliver most of the drug because of the drying and concentration of the solution during nebulization. As much as half the initial dose has on occasion been recovered from the nebulizer after it had been considered that the treatment was completed.

Sodium penicillin was administered in 30,000 unit doses in 15 cc of saline. Administration usually required from one to one-and-one-half hours. None

TABLE III  
PENICILLIN THERAPY

Time	Serum Level (U/cc)
$\frac{1}{2}$ hour	0.24
1 hour	0.18
$1\frac{1}{2}$ hours	0.09
2 hours	0.05

Penicillin serum levels in dogs following 20,000 U intra tracheally. Each value represents the average of three to eight determinations.

### Aerosol Penicillin - Serum levels

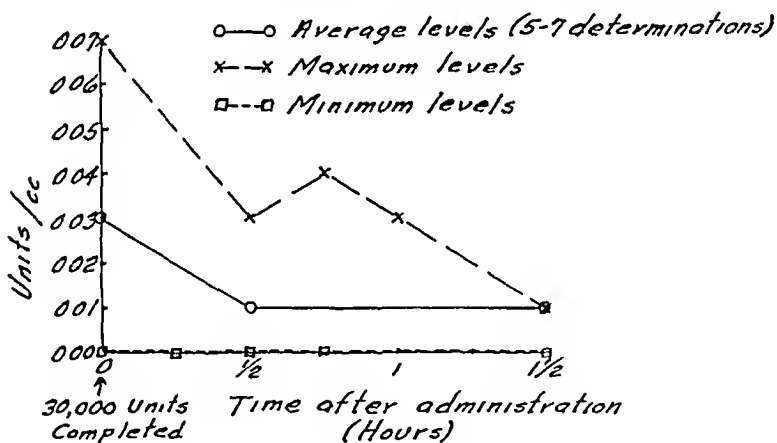


CHART 3—Blood serum levels (units per cc) at various time intervals following administration of 30,000 units of penicillin by aerosol.

of the patients complained of the taste, or of irritation of the upper respiratory tract. Blood serum levels appear in Chart 3.

Maximum serum levels were noted at the completion of administration, representing, on the average, only minimal therapeutic levels. From one-half to one-and-one-half hours after nebulization only traces of the drug were usually noted.

Aerosol penicillin was attempted on 10 dogs, usually delivered through a positive pressure anesthesia apparatus. Some of the dogs were normal, others were undergoing pneumonectomy at the time of administration. The usual dose was 16,000 units, corresponding by weight to about 70,000 units in man. With one or two exceptions blood serum titers showed at most a trace of

penicillin Synchronizing nebulization with respiration was not attempted, and much was doubtless lost in both exhaled mists and at angular points in the apparatus, disturbing a smooth air flow

#### D Intrapleural Administration

*Serum levels* Penicillin was administered intrapleurally and blood serum assayed for penicillin in eight patients Assay determinations are represented in Chart 4

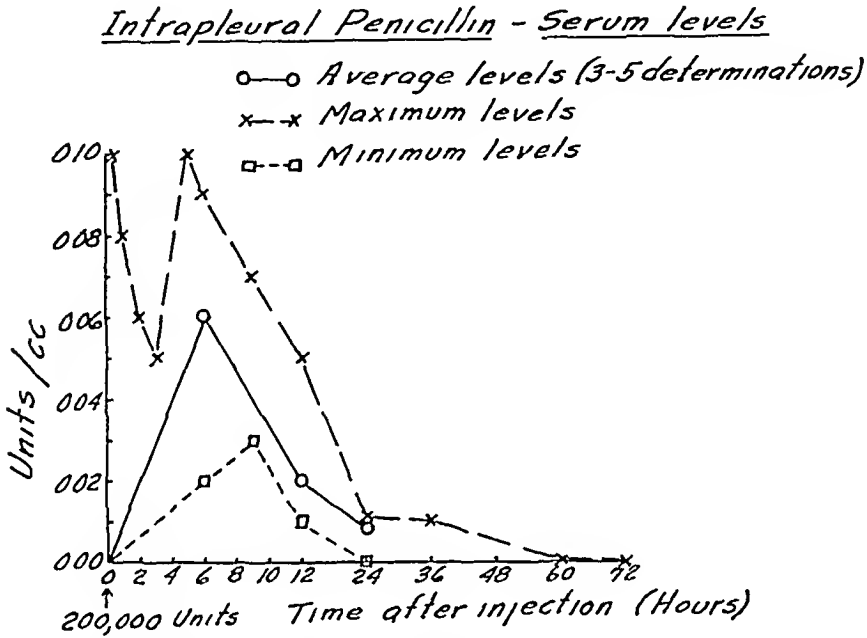


CHART 4—Blood serum levels (units per cc) at various time intervals following intrapleural administration of 200,000 units of penicillin

Administration of the drug was by thoracentesis, or following pneumonectomy it was combined with 500 cc of plasma instilled into the empty pleural cavity No appreciable difference in serum penicillin levels were observed from the two technics, and the results are combined Therapeutic levels were present in the serum for 9 to 12 hours with traces detectable up to 36 hours after injection

The curve representing maximum penicillin levels was made almost entirely through the first 24 hours from determinations on one patient after a single intrapleural injection The jump in concentration occurring between the third and fifth hour is unexplainable unless one assumes an increased rate of absorption from the pleural cavity, or a diminished urinary excretion during that time Certainly a wide range of serum penicillin values through the first 12 hours is noted in the present studies

The curve of maximum values indicates that absorption of penicillin takes place from the pleural cavity sufficiently rapid to give therapeutic serum levels within the first half hour, rather than at six hours, as is suggested by the average curve



*Pleural fluid levels* Penicillin concentrations in the pleural fluid following intrapleural administration of 200,000 units are represented in Chart 5. Extremely high titers were found immediately after injection, as is to be expected. Average levels were seen to be maintained at good therapeutic values through at least 60 hours, and individual determinations at 84 and 114 hours still showed 0.38 units per cc and 0.21 units per cc respectively.

Intrapleural instillation of penicillin was made into the pleural cavities of ten dogs sometime following pneumonectomy and of two dogs at the time of pneumonectomy. The dosage was 50,000 units in 200 cc of pooled human

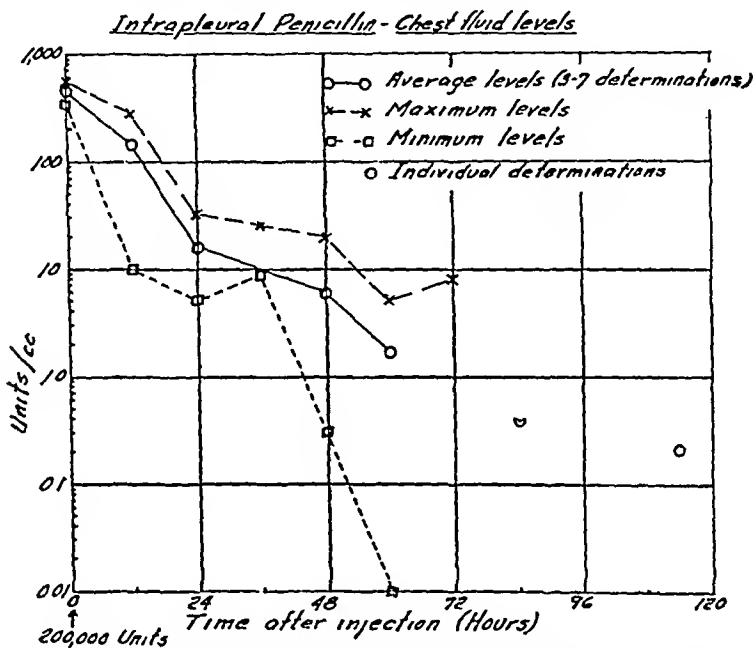


CHART 5—Penicillin titers (units per cc) in the chest fluid at various time intervals following intrapleural injection of a 200,000 unit dose

plasma. Chest fluid and blood serum assays revealed values in no way comparable to those in humans. Serum levels were extremely variable, ranging from 0.03 to 1.5 units per cc within the first five hours, and from 0.00 to 0.12 units per cc at about seven hours. At 24 hours no penicillin was detectable in the serum of any of the twelve animals. (Compare with Chart 4.) Chest fluid levels were also erratic, ranging from 2.90 to 44.0 units per cc within the first four hours, and from 0.10 to 1.80 units per cc at about seven hours. At 24 hours the chest fluid contained no detectable penicillin in any of the 12 dogs. Evidently penicillin is absorbed from the pleural cavity much more rapidly in dogs than in man.

#### DISCUSSION

The serum levels of penicillin resulting from use of the technics here studied are represented in Chart 6. The curves drawn represent the average values as shown on Charts 1, 2, 3 and 4.

Intramuscular penicillin generally gives the highest serum titers of the methods here studied, and is the most efficient routine method of administration for maintaining adequate serum levels. It has the disadvantage of frequent, rather painful injections, thus unpleasant for the patient and for the nursing staff. Doses larger than 20,000 units, or more frequent administration than once every three hours, would prevent serum concentration from falling to zero between injections and would be indicated for patients not responding well to the more conventional dosage schedule.

Intratracheal penicillin in 50,000 unit doses yields relatively poor and transitory serum levels. It could not ordinarily be used as a routine method of administration because of the technical difficulty involved and the discomfort

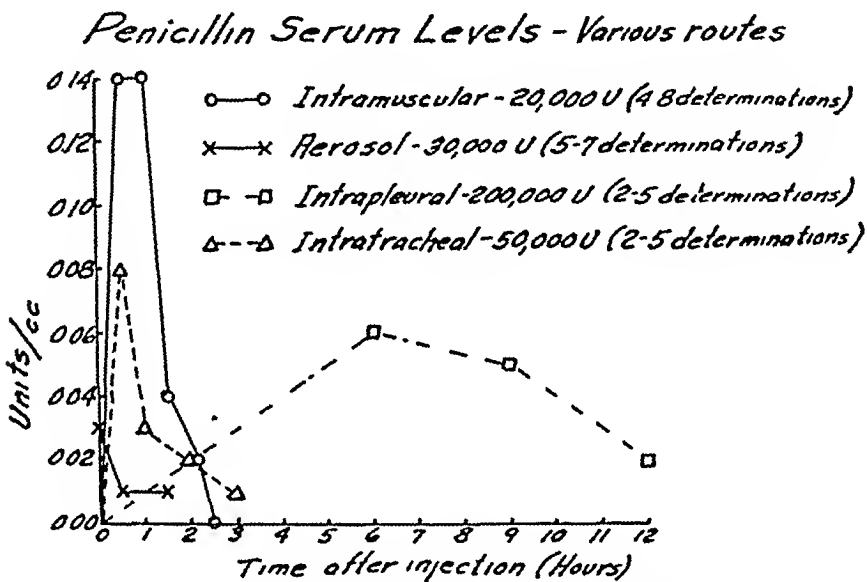


CHART 6—Penicillin serum levels (units per cc) at given time intervals following administration by various routes

to the patient. In patients with chronic bronchitis, asthmatic bronchitis, bronchiectasis or chronic lung abscess it may be of value in its local effect on the disease process. Kay and Meade<sup>10</sup> report intratracheal penicillin to be of particular value in the treatment of chronic bronchitis, minimal bronchiectasis, advanced inoperable bronchiectasis and in preoperative preparation of lobectomy patients. In many of their patients they noted a more rapid and more marked improvement than had been observed by the use of intramuscular administration of 25,000 units every three hours.

Aerosol administration of 30,000 unit doses of penicillin yielded the poorest serum concentrations of all the methods studied. Here again, except for the possible local effect of the drug in diseases of the bronchial tree it would not be indicated as a routine method of therapy. The concomitant oxygen therapy may be indicated for some patient, but unfortunately in these same individuals one could not expect the cooperation or ability necessary for efficient utilization, as is required for the technic described above. A nasal

catheter has too small a diameter to be an efficient conduit for the mists, and a large share of what should reach the respiratory tract would doubtless be exhaled, as was noted with ordinary breathing. The BLB mask is not an efficient medium for aerosol therapy in the limited experience of the authors. Mutch and Rewell<sup>11</sup> report high blood titers of penicillin using approximately 200,000 to 300,000 unit doses administered in one-half hour administrations, using a Collison nebulizer and BLB oxygen unit, and running eight to ten liters of oxygen per minute. They report wastage of 60 to 75 per cent of the solution. Barach, *et al*<sup>8</sup> and Vermilye<sup>12</sup> found relatively low serum concentration of penicillin following aerosol therapy, but they cite case histories in which distinct clinical improvement seemed directly attributable to this method of administration. It would seem wise to avoid considering aerosol penicillin as a panacea for the treatment of chronic infectious diseases of the respiratory tract until more data has been accumulated as regards the blood penicillin levels, to indicate a distinct advantage in this type of therapy. Aerosol is certainly not a substitute for intramuscular injections in conditions in which an adequate serum penicillin level is desired. If it is used indiscriminately in general practice and in the home, where Vermilye implies it should be of great value, it may easily result in great waste of the drug, needless expense and office visits for the patient and a false sense of security in the treatment given.

A clinical study of penicillin used by the aerosol method of administration was carried out by Dr. Erwin Levin of our Medical Department following the completion of the present study. This method of administration was used in 34 patients having bronchiectasis, chronic bronchitis or carcinoma of the lung. In some patients it was used as a means of treating active infection. In others it was used as a means of preparing the patients for operation. The usual dosage was 50,000 units of penicillin in 2 cc. of saline solution administered over a period of 20 minutes. This dosage was repeated every three hours five times a day for one to several weeks. In 21 of the patients all of the gram positive organisms disappeared from the sputum, and in 13 the number of these organisms was markedly diminished. Of the 11 patients prepared for operation by aerosol treatment for three to seven days, only two showed the presence of gram positive organisms in the surgical specimen. In six other patients the gram positive organisms disappeared from the sputum but returned in three to five days after the penicillin was discontinued. Of ten patients with chronic bronchitis treated by this method, nine showed little or no improvement. Doctor Levin's conclusion was that aerosol administration was an effective method for gram positive organisms in the sputum and was useful as a preoperative measure. About 20 per cent of these patients developed a rash or a glossitis or pharyngitis four to seven days after the treatment was begun. The treatment required the co-operation of the patient.

Intrapleural penicillin in 200,000 unit doses gives a sustained serum concentration at therapeutic levels for nine to 12 hours after administration, evidently rising to adequate levels within the first hour rather than over the

first six hours as indicated in Chart 6. Intrapleural injection is limited in its usefulness because its local effect in the pleural cavity is its primary objective, thus its use is limited to patients in whom fluid already exists in the pleural cavity, or following surgery such as pneumonectomy in which prophylaxis against empyema is desired. In several patients it was used concomitantly with intramuscular injections, and isolated serum assay suggests an additive, or even what might be called a symbiotic, effect from the two techniques, i.e., higher penicillin concentrations sustained for longer periods of time than might be expected from a simple summation of titers. There is insufficient data to consider this as more than a suggestion, however.

Pleural fluid penicillin levels following intramuscular injection are generally adequate following 20,000 unit doses, but more efficient use of the drug is apparent with 40,000 unit doses. From the limited data here presented it is evident that intramuscular penicillin, 40,000 units every three hours, would adequately control pleural infection by penicillin-sensitive organisms.

When thoracenteses are indicated for removing excess pleural fluid, where the chest is surgically or otherwise open, or when more resistant infectious organisms are encountered in the pleural cavity, intrapleural administration is preferred because of its great local concentration, absence of frequent painful injections and duration of action.

We have used this method of administration in 18 patients following total pneumonectomy for carcinoma of the lung, and in two patients with pulmonary suppurative disease. The only complication of empyema resulted following one of the two resections for pulmonary suppuration. In this patient a draining sinus was present at the time of pneumonectomy, thus contamination of the pleural cavity was considerable during the operation. This patient did not develop a bronchial fistula. One of the 18 patients with carcinoma of the lung developed a temporary bronchial fistula which healed spontaneously without the production of an empyema. One of the patients died of bronchial pneumonia in the remaining lung, but without a bronchial fistula or empyema on the side of surgery.

Intrapleural injections once every three days should be adequate for maintaining high therapeutic levels. When penicillinase-forming organisms\* are present in a mixed infection empyema, therapy should be directed at eliminating these organisms first, otherwise the penicillin may be rapidly inactivated, the resistant organisms may keep the infection active, and there is danger of penicillin resistance developing in the otherwise sensitive organisms due to prolonged exposure to non-bactericidal fluid levels of the drug.<sup>13</sup>

#### CONCLUSION

Intramuscular injection of penicillin is probably the best of the methods here studied as far as obtaining desirable blood serum levels in the non-surgical patient.

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\* *E. coli*, *Proteus vulgaris* and other gram negative motile bacilli are often potent penicillinase formers.

Intramuscular injections of 40,000 units of penicillin every three hours maintains good therapeutic levels in the pleural fluid. Twenty thousand unit doses appear much less effective.

Intratracheal instillation of 50,000 units of penicillin gives therapeutic serum titers at one-half hour but falls to minimum therapeutic levels by one hour. Doses of 100,000 units and 200,000 units give correspondingly higher serum values within the first hour after administration.

Aerosol penicillin in a dose of 30,000 units yields generally poor, but sometimes therapeutically adequate serum levels for as much as an hour after completion of administration. Larger doses would probably produce somewhat higher values. This technic is not to be regarded as a substitute for more established forms of administration in routine use, and until more efficient technics of utilization are developed and proved, aerosol penicillin should not be regarded as a home or office panacea.

Penicillin injected intrapleurally in 20,000 unit doses maintains therapeutically adequate serum levels for nine to 12 hours. Pleural fluid levels remain high for as much as four or five days after administration by this method.

#### SUMMARY

Several technics of penicillin therapy were studied, using serum and pleural fluid drug concentrations as primary criteria for evaluating the relative efficacy of treatment in thoracic surgical diseases.

(We are indebted to Mrs. Virginia Green, PhB, for the organization of the bacteriologic work and to Miss Mary Augustine, BS, for the penicillin assay determinations.)

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DISCUSSION—DR JOHN H GIBBON, JR., Philadelphia I think this work of Doctor Adams' is very important. It brings up the whole question of whether you should use antibiotic therapy locally, or generally, or combine both methods. The only way to answer the question is to study the concentrations of the antibiotic agent in the local fluid and in the blood serum. I think Doctor Adams has shown very well that there is some value in introducing penicillin into the pleural cavity after a pneumonectomy. We have been using penicillin in this fashion routinely. In 17 pneumonectomies for carcinoma performed in the past ten months we have had one empyema, and that was due to *B coli*.

I think his observations on aerosol penicillin are very interesting, and probably indicate that the procedure is not of great value in chronic pulmonary disease.

DR, ALFRED BLALOCK, Baltimore I have enjoyed the report of this excellent study by Doctor Adams and his associates. I wish to ask a question about the choice of patients in whom one should use penicillin. We have given penicillin routinely preoperatively and for the first few days postoperatively to approximately 400 patients with congenital heart disease upon whom we have operated in the last two years. We have had no instances of empyema or mediastinitis in this group, and I have often wondered if the penicillin is responsible for the absence of infections. At the same time I have worried about the expense and the discomfort which the injections cause. Being somewhat superstitious in nature I have hesitated to discontinue this routine practice of giving penicillin to this group of patients. I wonder if Doctor Adams would express an opinion as to whether such injections should be given routinely.

DR W E ADAMS, Chicago (closing) I do not think I am in any better position to answer Doctor Blalock's question than he is, or others here. We have felt likewise that penicillin is used more frequently than is necessary. The problem is, when to use it. If there is any possibility of respiratory function being interfered with following operative procedures, from collapse of the lung or less expansion of the lung than normal, and some likelihood of atelectasis or pneumonitis, this would be an indication to use it. These may frequently occur in thoracic surgery. We are using penicillin at the present time in all thoracic surgery and in much of our general surgery.

When we started this study we hoped that the aerosol method would prove to be more efficient than it has. All patients dislike being stuck every three hours with intramuscular injections, but since the blood serum levels of the aerosol method were so poor, we felt it was not a good substitute for the intramuscular method. At the present time we use penicillin intramuscularly to prepare patients for operation, and immediately after operation until the temperature is down to normal, following this we depend on the intrapleural method for the most part. I share Doctor Gibbon's view regarding the poor results of the aerosol method in chronic pulmonary infections.

I want to thank Doctor Gibbon and Doctor Blalock for their discussion.

## STUDIES IN POSTOPERATIVE CONVALESCENCE<sup>†</sup>

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IT HAS BEEN only during the past 10 or 15 years that the surgical profession has fully appreciated the true value of proper preoperative and postoperative care in the treatment of patients undergoing operation. In general, so much more attention has been devoted to preoperative than to postoperative care that efficiency of treatment of the latter type has lagged behind. Although various therapeutic procedures carried out in preoperative care can and must be continued on into postoperative care, there are many types of therapy which are very important in the after-care of patients, but of unknown or little significance in preoperative care. Ambulation is an example of this difference in value between certain types of treatment, since it plays a much greater role in postoperative care, although all surgeons appreciate the danger of operating on patients who have been bedfast for several days before operation.

Although as long ago as 1899 Ries<sup>1</sup> called attention to the value of ambulation in postoperative care, its true significance was not appreciated for three or four decades. The importance of ambulation and graded exercises in shortening convalescence in military personnel was noted by Rusk,<sup>2</sup> Karpovich<sup>3</sup> and others. However, the work done by the above authors applied primarily to convalescence from non-surgical disease. Furthermore, many of the exercises (including the Harvard step test<sup>4</sup>) used in the study of convalescence from diseases such as pneumonia, measles, scarlet fever, etc., cannot be utilized in surgical patients (particularly those having had a laparotomy) because of the danger of wound separation. On the other hand, ambulation can be utilized with safety in surgical patients as has been shown by the pioneer work of Powers<sup>5</sup> and others during recent years.

Considerable clinical data have been accumulated up to date revealing the advantages of ambulation. Economy of hospitalization is by no means the most important advantage. A comparative study of a large series of cases by Schafer and Dragstedt<sup>6</sup> has revealed a lower incidence of atelectasis and less postoperative fever in the ambulated patients. Leithauser<sup>7</sup> has reported that in ambulated patients the normal vital capacity returns in two to seven days instead of seven to 14 days in patients not ambulated, he considers that "pul-

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\* Read before the American Surgical Association, March 26, 1947, Hot Springs, Va.

† The work described in this paper was done under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and the University of Illinois.

monary complications increase in direct proportion to the reductions in vital capacities ”

Elman and Akin<sup>8</sup> have emphasized the deleterious effect of bed rest and malnutrition on appetite and accordingly have very aptly warned that by no means can appetite be considered an index of the patient's caloric needs. Preliminary reports on ambulation suggested that it would eliminate phlebotrombosis and pulmonary embolism. However, Powers<sup>5</sup> has reported that venous thrombosis is by no means eliminated, although the incidence of fatal pulmonary embolism appears to be reduced. Burch and Fisher<sup>9</sup> report two fatal pulmonary emboli in 1908 patients ambulated after abdominal operations at an army hospital. This appears to be a low incidence, but when we realize that practically all of these patients (representing a group in which pulmonary emboli are relatively infrequent) were young, it becomes obvious that these complications will not be eliminated by ambulation. Numerous observers have reported an improvement in wound healing with a lowered incidence of wound disruption.

The presence of a negative nitrogen balance in convalescing patients has long been known. Cuthbertson's<sup>10</sup> early observations (1932) that the nitrogen excretion on the first postoperative day is low has been confirmed by the authors and others. Cuthbertson reported further that the negative nitrogen balance following operation exceeded that observed during starvation, indicating that lack or decrease of food intake was not the only factor giving rise to a negative nitrogen balance in patients convalescing from operation. Merely confinement to bed has been shown to result in a negative nitrogen balance (Keys<sup>11</sup>). Elman and associates<sup>8</sup> and Co Tui and associates<sup>12</sup> have called attention to the fact that the postoperative negative nitrogen balance in patients can be prevented by force feeding with proteins and parenteral administration of amino acids. However, it is well known that a simple order to force feedings in patients immediately postoperatively cannot solve the problem of negative nitrogen balance because of the gastric and intestinal atony so commonly observed following laparotomy. The conclusion expressed by Ivy and Grossman<sup>13</sup> that “the best means for increasing gastric tone and motility is physical exercise” can be supported by all observers studying patients during postoperative convalescence.

#### PURPOSE OF EXPERIMENTS

Unfortunately the pendulum always swings too far when a new form of therapy is introduced, unquestionably many patients are harmed in vigorous ambulation programs, by the uncontrolled efforts of some surgeons not too well informed on physiologic functions and the inadequate reserves of their patients. As a matter of fact, very little data are available at the present time to indicate which patients should not be ambulated, and how much ambulation should be prescribed. Furthermore, ambulation is only one of innumerable forms of treatment which might be instituted to improve the rate of post-



operative convalescence We are already becoming aware of the great value of a high protein intake (Elman), and liberal quantities of blood Other factors, including chemotherapy, physiotherapy, psychotherapy, etc., are important in convalescence but without doubt many other types of therapy still unknown may aid greatly in the speed of recovery from operations

However, we cannot expect other important discoveries to be made in the field of postoperative convalescence without first getting more data as to what physiologic functions are impaired and how Perhaps one of the most important questions to solve is the explanation of the extreme weakness so prevalent following major operations, particularly in people past middle age Inadequate diet will explain many decrements, as will be discussed later, but is not the major factor in explanation of this manifestation, which is probably the most important one retarding convalescence Has the cardiac reserve been impaired sufficiently to explain this weakness and fatigue? At present there is inadequate evidence to explain these symptoms on that basis Has the content of glycogen or other tissue constituents in the muscle been disturbed sufficiently to explain them? Could impairment of such organs as the liver, adrenal glands, etc., explain them? It is obvious that the true explanation is unknown

For reasons discussed above there is an obvious need for the study of (1) the functions of various organs during convalescence and (2) additional factors in therapy which may prevent the various insufficiencies produced by major operations It is for these reasons that the experiments herein discussed were undertaken

#### DESCRIPTION OF TYPES OF THERAPY

**DIVISION OF PATIENTS INTO GROUPS**—In our efforts to determine what types of therapy might improve the rate of convalescence we divided the patients into a number of groups, each of which varied in the type of therapy The first 14 groups listed below consisted entirely of patients having herniotomy, most of these patients were relatively young men The last two groups consisted of patients having cholecystectomy All groups not designated as "full diet daily" had no oral feeding the day of the operation, and 1/4, 2/4, 3/4 and 4/4 of their diet on the first 4 postoperative days respectively

(I) *Control hospital group*—This group of patients was chosen from the surgical floor and served to furnish scout data None of these data were utilized in actual computation of results in the various groups

(II) *Control Experiment Group*—In utilizing data described in Group I, we decided that the diet for our control patients should contain basal calories plus 20 per cent, 15 per cent\* of which were derived from protein This might be considered barely sufficient for maintenance

(III) *"Shotgun" Group Supplements,\*\* basal diet plus 100 per cent with 20 per cent protein full diet daily, ambulation†*—In planning for the treatment of this group the objective was to furnish all factors that might conceivably influence convalescence favorably The diet consisted of basal calories plus 100 per cent, with 20 per cent of the calories from protein This diet was served preoperatively in the form of meals On the day of operation and on the succeeding postoperative days, until the patient was again able to eat, it was given in the form of a tube feeding This insured the maintenance of the nutrition at a constant level

\* The figure designating percentage protein refers to per cent calories, not weight

\*\* Data on the quantity of the various supplements will be included in another publication in preparation

† All groups not designated "ambulation" were not ambulated

Preoperatively the diet contained the following supplements: choline, vitamin B complex from yeast, Ascorbic acid, Vitamin A and Vitamin D. On the day of surgery and on the four succeeding postoperative days the following supplements were given parenterally: Vitamin K, Liver extract (2 units to 1 cc), Adrenal cortical extract, Testosterone propionate, Thiamine chloride, Riboflavin, Pyridoxine, Calcium pantothenate, Nicotinamide, Ascorbic acid and Choline.

In addition to the above supplements, methionine and 5 per cent amigen solution in 5 per cent glucose (2000 cc intravenously) were given on the day of surgery. This group received ambulation. Early in the study of this group it was obvious that the "Shotgun" group had reacted favorably to the treatment. Consequently, the groups described below were set up to analyze the factor or factors responsible for this favorable effect.

(IV) *Basal Calories Plus 20 per cent, 15 per cent Protein, Spinal Anesthesia*—This group was maintained in bed without any form of exercise. The effect of inhalation anesthesia was eliminated.

(V) *Basal Calories Plus 20 per cent, 15 per cent Protein, Spinal Anesthesia, Modified Ambulation*—These patients received push-up, step-up and psychomotor tests. It is realized that this program gave the patients a certain amount of ambulation.

(VI) *Basal Calories Plus 20 per cent, 15 per cent Protein, Ambulation*

(VII) *Basal Calories Plus 20 per cent, 15 per cent Protein (Full diet given each day, by tube for first few postoperative days)*

(VIII) *Basal Calories Plus 20 per cent, 15 per cent Protein, Supplementation*—The supplements were the same as those described above under "shotgun" group (III) except that vitamin K, 4 mg, was administered throughout the hospital stay.

(IX) *Basal Calories Plus 20 per cent, 15 per cent Protein, Methionine*—Two grams of methionine was administered daily from the date of entrance.

(X) *Basal Calories Plus 20 per cent, 15 per cent Protein, No Surgery*—These patients were kept in bed, given the same food, fluid, and sedation as group II but herniorrhaphy was omitted. The patients were quite young, 16 to 17 years of age, which suggests that they may not be entirely comparable with the other groups.

(XI) *Basal Calories Plus 20 per cent, 40 per cent Protein (Full diet given for each day, by tube for first few postoperative days)*—This diet increased rather sharply the protein intake. It ranged between 182 and 233 Gm with an average value of 201 grams.

(XII) *Basal Calories Plus 20 per cent, 40 per cent Protein (Full diet given each day, by tube for first few postoperative days), Ambulation*

(XIII) *Basal Calories Plus 100 per cent with Protein at the Control Level*—This group was planned to test out the effect of excess calories from sources other than protein. The protein was the same as that in the control diet containing basal calories plus 20 per cent. Since the calories in the diet were increased, the distribution of the constituent factors was altered. The diet now derived 10 per cent of its calories from protein and 40 per cent from fat. On the day of surgery the patients received no protein, on the first postoperative day 1/4, second, 2/4, third, 3/4, and fourth, 4/4 of the prescribed daily protein.

(XIV) *Basal Calories Plus 40 per cent, 15 per cent Protein*—This group was composed of women having herniotomy who were placed on the regime used in patients submitted to cholecystectomy. This plan furnished an opportunity to make a comparison of the relative loads of cholecystectomy and herniotomy. More specifically, it served as a control group for the later studies in alterations in serum proteins found in patients undergoing cholecystectomy.

(XV) *Cholecystectomy, Basal diet plus 40 per cent, 15 per cent Protein, General Anesthesia*—This group might be considered the control group for cholecystectomy.

(XVI) *Cholecystectomy, Basal diet plus 40 per cent, 15 per cent Protein, Spinal Anesthesia*—This group is the same as XV except that spinal anesthesia was used instead of ether anesthesia.

#### EXPERIMENTAL METHODS

In the experiments herein discussed, we have limited our study to patients having herniotomy or cholecystectomy. Studies are also being made in other types of operations, particularly those in which more operative work is required—(e.g. gastrectomy). However, most of the work was done on patients having herniotomy because they lend themselves so well to experimental study, the preoperative condition of the patient is so stabilized, and the amount of operative work so nearly equal in all cases. The preoperative period consisted of 4 to 7 days and was devoted to tests on the patients and

to stabilization of their diet. The control group of patients was allowed out of bed on the 10th postoperative day and discharged on the 12th day. Those in the other groups, who did not receive ambulation, were out of bed on the 6th postoperative day and were discharged on the 7th day. Those who received ambulation were out of bed on the 1st postoperative day and discharged on the 7th day.

**DIETARY MANAGEMENT AND FLUIDS**—Large quantities of basic foods were procured, analyzed for nitrogen, weighed and placed in a deep freeze unit maintained at minus 10°F. Tube feedings consisted primarily of evaporated milk, skimmed milk powder, amigen and dextrose. Low protein diet consisted of salad oil (one egg yolk per 200 cc), glucose and water, it containing 3.2 Gm protein and 3020 calories per liter.

**Herniotomy**—On the day of operation the control herniotomy patients were given 1000 cc of physiologic saline and 1000 cc of 5 per cent glucose intravenously, nothing was given by mouth. On the succeeding days they were given 1/4, 1/2, 3/4 and 4/4, respectively, of their postoperative diet.

**Cholecystectomy**—A stomach tube was inserted for decompression, it was removed at the end of the second postoperative day. On the day of the operation the cholecystectomy patient received 1000 cc of 5 per cent glucose in physiologic saline and 2000 cc of 5 per cent glucose intravenously. The same fluids were given on the first and second postoperative day except that when the amount of fluid aspirated from the stomach exceeded 500 cc per day, an amount of 5 per cent glucose with saline was given to equal the excess beyond 500 cc. On the third postoperative day the patient received 1000 cc of 5 per cent glucose or physiologic saline intravenously and 600 calories by mouth. The diet was increased 600 calories per day until the patient was receiving his preoperative diet, 1 e basal diet plus 40 per cent.

**EXERCISE AND AMBULATION**—In the group of patients subjected to ambulation we added calisthenics similar to those described by Stafford, DeCook and Picard<sup>14</sup>. Preoperatively the patients were given calisthenics for 21 minutes each day, divided into two periods. Postoperatively they were given calisthenics for 20 minutes divided into 2 periods. The "sit-up" exercises which were given preoperatively were omitted postoperatively because of the danger of damage to the wound. In addition to the calisthenics the patient was out of bed each day for a period increasing with each postoperative day.

**ANESTHESIA**—General anesthesia consisted of nitrous oxide and ether administration. Tracheal intubation was used uniformly. The same preoperative medication was utilized in all cases, namely morphine and scopolamine. Pontocain was used for spinal anesthesia.

**TESTS UTILIZED**—Innumerable tests were chosen to be carried out on the patients but preliminary work proved many of them unsatisfactory for several and varied reasons.

**Liver function tests**—The *urobilinogen test*, as performed by Watson, proved to be one of the most satisfactory tests of liver function. The test depends upon the quantitative excretion of urobilinogen in the urine, expressed in milligrams excreted in 24 hours.

The *bromsulphalein test* was also effective in determination of the hepatic function. Five milligrams per kilo of body weight of bromsulphalein were injected intravenously and samples of blood drawn at 30 minutes and at 40 minutes. The sum of these two readings was chosen as the method of arriving at one figure for recording results of the tests. Postoperative values were expressed in terms of percentage of normal preoperative efficiency.

Numerous miscellaneous tests of liver function were used. The *prothrombin test* (Quick) was utilized, and as illustrated later, yielded information of variable value. The *cephalin flocculation test*, the *hippuric acid test*, the *galactose tolerance test* and *bilirubin excretion test* were used but did not appear satisfactory or adaptable for our purpose and were abandoned after preliminary trial. The two-dose *Erton-Rose glucose tolerance test* was also utilized but not found adaptable except in the patients submitted to cholecystectomy. Blood sugar was determined in the fasting state and at the end of one-half hour, one hour and two hours after the first dose of glucose.

**Metabolic tests**—Nitrogen balance studies were carried out on all patients and, as has been shown by numerous authors, proved to be of great value. The nitrogen in the urine and food was determined by the macrokjeldahl method with titration of the ammonia. In computing the nitrogen balance, it was assumed that the fecal nitrogen was equal to 10 per cent of the ingested nitrogen.

**Serum total proteins, serum albumin and serum globulin** were determined in only one group of patients submitted to herniotomy but in both groups submitted to cholecystectomy. These determinations were made by standard procedures.

**Serum total cholesterol and cholesterol esters** were determined by using digitonine separation technic.

The determination of *17-ketosteroids* was carried out after the technic described by Robbie and Gibson

Quantitative tests were performed for *creatinine* and *creatin excretion*, but as indicated later results yielded no significant data

*Circulatory efficiency and muscular fitness*—A *tilt-table test* was carried out on several groups of patients. The procedure and method for scoring performance will be described in a paper soon to be published

Recently a *modification of the flarimeter and Flack test* has been used\* to study cardiovascular reserve or function. In general, the procedure consists of determining the cardiovascular response to an increase in intrapulmonary pressure obtained by having the patient blow against a resistance of a column of mercury, and maintaining this pressure for a specified period of time. Blowing in this manner exerts pressure on the thin-walled superior and inferior vena cavae, and on the pulmonary veins, thus interfering with the filling of the right and left auricles respectively. It would appear that this procedure would test the ability of the vascular system to compensate for a reduced cardiac output brought about by obstruction to the flow of blood through the vena cavae and pulmonary veins

All tests were performed one hour or more after breakfast and immediately following one half-hour of complete bed rest. The procedure was carried out with the patient in two positions, namely, supine on the tilt-table, and then with the tilt-table tilted to an angle of 60°. The apparatus consists of a mouthpiece attached by appropriate thick-walled rubber tubing attached to an aneroid manometer possessing a large recording dial, which the patient may observe, thus aiding him in maintaining the required level of pressure. A side tube was introduced into the system, the free end of which was filled by a metal disk containing an opening  $\frac{1}{64}$  inch in diameter. This vent for a constant escape of air is necessary to prevent the patient from maintaining the pressure with the muscles of his mouth or pharynx

After obtaining a series of control blood pressure and pulse rate readings in the supine position, the patient is instructed to take a very deep inspiration and blow into the system to raise the pressure to the desired level of either 20 or 30 mm Hg. In each instance the patient continues to blow for 25 seconds. Blood pressure readings are obtained at the end of 10 and at the end of 20 seconds of blowing, immediately after the procedure is terminated, 20 seconds later and, if necessary, 1 minute later. Instead of recording pulse rates during the period of blowing and in the period of recovery, a more accurate count can be obtained by using Lead II of the electrocardiograph. The test is repeated with the patient tilted at an angle of 60°

A *push-up test* was devised to obtain readings following strenuous exercise of the upper extremities which would not endanger the abdominal wound. A weight lifting apparatus on a frame was designed to fit over the bed so that the patient could lie on his back and push up two weights of 20 pounds each. The weights were raised at the rate of 30 times per minute for two minutes. In scoring the test the resting pulse rate was compared with the pulse rate obtained at 5 second intervals for 3 minutes, starting 5 seconds after the end of the test. The difference between the resting pulse rate and the rate obtained between the interval of 5 to 35 seconds and 60 to 90 seconds was recorded as the result of the test. The apparatus could be used as a form of ambulation, or as a test for circulatory efficiency. When used as a test, it was applied three or four times preoperatively, on the first postoperative day and continued on succeeding days

The *flarimeter test* was performed on a few groups of patients. The patient took three long preliminary inspirations and expirations. He then inspired maximally and at the 4th expiration maintained an expiratory pressure of 40 mm mercury as long as possible. This is a different test than the modified flarimeter-Flack test previously described

The *vital capacity* was determined by a Collins Spirometer on a few groups of patients

The *strength of hand grip* was determined by the Smedley hand dynamometer. The highest of four trials given at 30 second intervals was used as the maximum. *Endurance time* was also determined with the dynamometer. This represented the length of time the patient could maintain a grip equal to 40 per cent of the maximum strength of the hand grip

*Psychomotor tests*—Tests including steadiness of hand, speed of tapping, simple choice reaction time and coordination time were done on many patients with herniotomy, but since the results were insignificant the tests were discarded early in our

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\* Tests modified by Dr. David Abramson, who has recently joined our group studying convalescence

studies For a time we utilized the critical fusion frequency of flicker test as a measure of determining fatigue of the retino-cortical system Results of this test were likewise of no statistical significance

STATISTICAL ANALYSIS—All data were submitted to a statistical analysis Whenever the term "significant" is used in the text, it is applied in the statistical sense

## RESULTS

LIVER FUNCTION TESTS—Of the numerous liver function tests used in our studies, the urobilinogen and bromsulphalein tests were of the most value

*Urobilinogen Test*—The average preoperative value for 92 patients with hernias was 1.61 mg for 24 hours Only 2 had a preoperative value of more than 4 mg The average preoperative level in 10 patients with cholecystitis was 1.19 mg We found that the postoperative level was influenced sharply by the preoperative level It therefore appeared most accurate to express the postoperative urobilinogen excretion in terms of a percentage efficiency based upon the preoperative value, the figure was obtained by dividing the preoperative value by the postoperative value and multiplying by 100 The values of the first 5 postoperative days were averaged to obtain the individual score The values of all the patients in each group were averaged to give a numerical value for the group

In the groups having ambulation or a high percentage of protein in their diet the postoperative excretion of urobilinogen remained at levels considered to be within normal limits or near normal Table I reveals that the best score in the hernia patients was made by the "shotgun" group, which had received numerous supplements and a basal diet plus 100 per cent with 20 per cent protein The percentage efficiency in this group was 109 compared to 60 in the control group operated on for herniotomy without any special therapy

TABLE I

Scores and ranks of the groups of patients with herniotomy based upon postoperative values expressed as percentage of preoperative values for urobilinogen bromsulphalein and tilt table and upon nitrogen balance in grams over a period of six days

Group	No of Pts	Management	Urobilinogen Excretion (Rank)	Bromsulphalein Retention (Rank)	20 Minute Tilt Table Response (Rank)	6-Day Nitrogen Balance (Rank)	Final (Rank)
XII	5	B+20% 40% protein, ambulation, tube fed*	86 (3)	89 (1)	103 (3)	19.4 (1)	1
III	5	Shot gun B+100% 20% protein, tube fed, supplements, ambulation	109 (1)	66 (4)	123 (2)	10.2 (2)	2
VI	7	B+20% 15% protein, ambulation	61 (6½)	68 (3)	129 (1)	-21.3 (7)	3
XI	7	B+20% 40% protein, tube fed*	96 (2)	54 (9)	84 (4)	7.6 (3)	4
VII	6	B+20% 15% protein, tube fed*	61 (6)½	66 (4)	80 (5)	-13.8 (4)	5
IV	6	B+20% 15% protein, spinal anesthesia	86 (3)	74 (2)	71 (9)	-31.3 (10)	6
XIV	4	B+40% 15% protein, gallbladder post-operative regime	60 (8)	47 (10)	73 (7½)	-16.2 (5)	7½
VIII	7	B+20% 15% protein, supplementation	64 (5)	63 (6)	54 (10)	-29.8 (9)	7½
IX	4	B+20% 15% protein, methionine	40 (10)	61 (7)	78 (6)	-24.3 (8)	9
XIII	3	B+100% 10% protein, tube fed*	29 (11)	40 (11)	73 (7½)	-17.5 (6)	10
II	10	Control B+20% 15% protein	60 (8)	60 (8)	50 (11)	-31.4 (10)	11
I	22	Control on hospital diet*	69				
V	7	B+20% 15% protein, spinal anesthesia, modified ambulation†	104	65			

The figures in parenthesis after each column represents rank of efficiency of treatment in that group as compared to others

B=Basal diet \* Tube fed=A full diet was given every day (by stomach tube for first 4 postoperative days) including day of operation † Not included in ranking

POSTOPERATIVE CONVALESCENCE

In the 5 patients having cholecystectomy which were used as controls (ether anesthesia) the efficiency score was only 48 compared to an average of 60 in the hernia controls, thus indicating a greater load in cholecystectomy than in herniotomy, in this small series of gallbladder patients, those operated on with spinal anesthesia showed less hepatic impairment than patients given ether

In Table II designed to show the effect of complications on urobilinogen excretion, the figures are expressed in mg per 24 hours, but not all groups are included Under each complication is given the average for the group in which the patient with the complication

TABLE II  
Urobilinogen Excretion in Mg Per 24 Hours in Patients with Complications

Complication	Preoperative Average (Mg )	Postoperative Day				
		1	2	3	4	5
Stitch abscess	1 9	4 5	14 9	36 4	45 7	27 8
Control group IX*	1 4	2 9	10 1	9 5	5 8	3 4
Wound infection	1 2	3 1	40 7	44 0	90 2	9 7
Control group III*	1 1	0 9	1 2	2 2	2 3	1 8
Pneumonia	1 1	19 3	17 0	6 7	3 3	2 4
Control group XI*	2 3	3 5	4 8	3 5	2 7	2 6
Atelectasis pneumonitis	6 7	15 4	18 6	2 8	2 1	1 5
Control group II*	2 6	3 9	4 6	5 5	6 3	4 7
Cystitis	1 8	1 4	5 9	16 7	8 2	
Control group IX*	1 4	2 9	10 1	9 5	5 8	3 4
Coronary thrombosis	1 9	1 6	6 3	6 2	9 1	9 4
Control group VIII*	1 3	2 1	2 5	3 0	2 6	2 4

\* Other members of same diet group who suffered no complications

was originally placed The marked increase in urinary excretion of urobilinogen in patients with complications is striking These results suggest that although the operation itself inflicts a definite load upon the liver, most postoperative complications inflict still a greater load The marked impairment in complications suggests that the test is a valuable index of hepatic efficiency

Another reason for considering the urobilinogen test an efficient one is the fact that the excretion remained above normal for 6 to 8 days postoperatively The maximum was usually noted on the 2nd postoperative day Improvement was gradual until the normal figure was regained

*Bromsulphalein Test*—Tests were run two times preoperatively and on the first, third and fifth postoperative days Postoperative values were expressed in terms of percentage of normal preoperative efficiency

Postoperative retention returned to normal by the fourth or fifth day contrasted to the persistence of abnormal excretion of urobilinogen for 6 to 8 days postoperatively

As was revealed by the urobilinogen test, ambulation and a diet with a high protein content reduced the postoperative impairment to a very low figure

TABLE III  
Urobilinogen Excretion in Control Patients Having Operation (Group II) Compared to Excretion in Patients Put Through Same Regime Without Operation (Group X)

Group Number	Management	Av Pre-Op Excretion in Mg Per 24 Hrs	Preoperative Per Cent of Postoperative Value Days of Postoperative Regime					
			1	2	3	4	5	6
II	Control	2 59	77	75	45	48	57	100
	Basal diet +20%	(Av of 10 pts)						
	15% protein							
X	Basal diet +20%	{	69	12	9	13	75	65
	15% protein		86	34	44	56	506	261
	Sedation		1 02	19	76			
	No operation (4 patients)		72	24	28			

TABLE IV  
Nitrogen Balance (in Grams) in Patients With Complications (Including the Day of  
Operation and 5 Succeeding Days)

Complication	Preoperative		Postoperative	
	Patient	Control*	Patient	Control*
Stitch abscess	-2 78	+2 80	-71 50	-24 29
Wound infection	+9 72	+4 16	-30 09	+10 24
Pneumonia	+3 57	+5 55	- 9 79	+ 7 62
Atelectasis	-2 49	-2 30	-49 86	-31 44
Cystitis	-0 85	+2 80	-39 57	-22 75
Coronary thrombosis	-0 55	-1 46	-25 30	-29 81

\* Other members of same diet group who suffered no complications

Table I reveals the best score in Group XII (Basal diet plus 20 per cent, 40 per cent protein and ambulation) The score in this group was 89 per cent of the preoperative efficiency as compared to 60 per cent in the control group (II) The fact that the degree of change in postoperative figures over preoperative figures was much less pronounced than with the urobilinogen test suggests that the urobilinogen test is superior to the bromsulphalein test as an indication of hepatic function As in the urobilinogen test, there was a decrease in efficiency of liver function in patients with complications, but the degree of inefficiency was much more marked in the urobilinogen test

*Miscellaneous Tests of Liver Function*—The *prothrombin test* in herniotomies revealed little positive information except a slightly greater tendency to remain nearer normal in patients having spinal anesthesia than in those having nitrous oxide and ether The *Exton-Rose glucose tolerance* test revealed higher blood sugar curves postoperatively than preoperatively but there was little difference between the two groups in which it was used, the test was therefore considered to be of only slight value in our experiments The *hippuric acid* test, *cephalin flocculation* test, *excretion time for bilirubin*, and the *galactose tolerance* test were used but were abandoned as not being as suitable or reliable as the urobilinogen and bromsulphalein tests

*METABOLIC TESTS*—Of the various tests in this group the most significant results were obtained in those dealing directly with the metabolism of proteins

*Nitrogen balance studies*—Analysis of figures on nitrogen balance reveal one major fact, namely that regardless of the procedures utilized to abolish decrements, a negative balance cannot be averted unless the patient is getting a certain amount of protein It is admitted, however, that a high carbohydrate or fat diet will have a tendency to spare protein

In Table V, the data showing the effect of ambulation and slight deviation in diet on nitrogen balance is summarized In Category A, the diet, basal plus 20 per cent with 15 per cent protein, was carried out without deviation in the group which was not ambulated, as well as in the ambulated group In the former group the nitrogen loss for the 6-day postoperative period was 31.4 Gm compared to a loss of 21.3 Gm for the latter group, indicating that ambulation actually tends to decrease the nitrogen loss The favorable effect is further substantiated by Category B containing 2 groups placed on identical diets, i.e. basal diet plus 20 per cent with 40 per cent protein The first group was not ambulated, the second group was ambulated The nitrogen gain was greater in the ambulated group, being 19.4 Gm for the 6-day period, compared to 7.6 Gm for the non-ambulated group In another series, designated as Category C, in which the diet was basal plus 20 per cent with 15 per cent protein for each group, a comparison is not valid because the ambulated group (VI) received only a partial diet during the first 4 postoperative days, this data merely indicates that ambulation is no substitute for protein or food Analysis of the other two groups illustrated in Table V indicate quite clearly that ambulation tends to decrease nitrogen loss

POSTOPERATIVE CONVALESCENCE

A comparison of the figures on nitrogen balance between groups IV and II in Table I indicates that spinal anesthesia has no sparing effect on nitrogen. Each group had the same diet, all therapy being the same except that Group IV had spinal anesthesia while Group II had gas-ether anesthesia. The nitrogen loss was identical, being 31.3 and 31.4 Gm respectively for the 6-day period. This conclusion is substantiated by the two group studies in patients having cholecystectomy. Each of the 2 groups had the same diet

TABLE V  
Effect of Ambulation and Slight Deviation of Diet on Nitrogen Balance

Category	Diet		6 Day Nitrogen Balance
A	Basal diet +20% 15% protein Partial diet First 4 P O days	(Group II) (No ambulation)	-31.4 Gm
		(Group VI) ambulation	-21.3 Gm
B	Basal diet +20% 40% protein Full diet daily	(Group XI) no ambulation	7.6 Gm
		(Group XII) ambulation	19.4 Gm
C	Basal diet +20% 15% Protein	(Group VII) no ambulation Full diet daily	-13.8 Gm
		(Group VI) ambulation Partial diet first 3 P O days	-21.3 Gm

(namely basal plus 40 per cent with 15 per cent protein) and all other factors equal except that one had spinal and the other gas-ether anesthesia. The nitrogen loss in the two groups was almost identical, being 31.1 and 29.0 Gm respectively for the 6-day period.

*Serum total protein, albumin and globulin*—Realizing that an herniotomy was probably not a sufficient operative load to produce a decrease in serum proteins, we analyzed the blood for protein in only one group of hernia patients, namely those having a basal diet plus 40 per cent, 15 per cent protein (Group XIV). The postoperative decline in serum albumin and total protein was of statistical significance on the third day (see Table IV), but was only 13 and 9 per cent respectively below the preoperative level.

However, following cholecystectomy the reduction was of definite statistical and clinical significance (see Table VI). In the group having ether anesthesia, the serum albumin declined gradually until by the 11th day the value was only 75 percent of the preoperative figure. The reduction in this group was definitely greater than in the group

TABLE VI  
Postoperative Changes in Serum Total Protein, Albumin and Globulin, Expressed in Percentage of Preoperative Level of Patients Submitted to Cholecystectomy and Herniotomy

Group Number	Management	Preoperative Avg in Gm /100 cc	Percent Pre-Op Level Postoperative Day			
			3	5	7	11
XV Chole- cystectomy	Basal diet +40%	Total Protein 6.47	92		90	89
	15% protein	Albumin 3.87	84		78	75
	Ether anes	Globulin 2.60	105		106	107
XVI Chole- cystectomy	Basal diet +40%	Total Protein 6.59	91	92	95	97
	15% protein	Albumin 4.14	82	82	87	91
	Spinal anes	Globulin 2.45	106	110	110	107
XIV Herniotomy	Basal diet +40%	Total Protein 6.75	91	93		
	15% protein	Albumin 4.26	87	89		
	Gallbladder postoperative regime	Globulin 2.49	98	98		



having spinal anesthesia In the latter group, there was a tendency toward an early recovery, by the 11th postoperative day the value had risen to 91 per cent of the preoperative level In the former group recovery was slow, several weeks elapsing before the preoperative level was reached The data indicate that ether anesthesia had a greater detrimental effect on blood protein than spinal anesthesia

In each group the globulin content rose slightly but not significantly, showing a slight tendency toward an A/G reversal, these findings support previous data revealing hepatic damage inflicted by operation

*Scrum total cholesterol and cholesterol esters*—Cholesterol determinations were made in one group of patients having herniotomy, namely Group XIV, which had basal diet plus 40 per cent, 15 per cent protein, with no supplements The values for total cholesterol

TABLE VII

Changes of Total Cholesterol Cholesterol Esters and Percent Cholesterol Esters in Patients Submitted to Cholecystectomy and Herniorrhaphy

Group Number	Management	Preoperative Average in mg /100 cc	Postoperative Average Day				
			3	5	7	11	
V	Cholecystectomy	Total cholesterol	254	193		213	229
	Basal diet +40%	Cholesterol esters	199	103		145	191
	15% protein	% cholesterol esters	78.5	53.4		68.1	83.4
	Ether anesthesia						
VI	Cholecystectomy	Total cholesterol	265	202	212	212	200
	Basal diet +40%	Cholesterol esters	212	162	165	178	171
	15% protein	% cholesterol esters	79.3	80.2	77.8	84.0	85.5
	Spinal anesthesia						
XIV	Herniotomy	Total cholesterol	246	224	238		
	Basal diet +40%	Cholesterol esters	216	185	208		
	15% protein	% cholesterol esters	87.8	82.6	87.4		

and cholesterol esters were significantly lower only on the third postoperative day (see Table VII)

In the patients having cholecystectomy there was a definite decline in the total cholesterol and cholesterol esters in both groups which were treated the same except for ether anesthesia in one group and spinal in the other The difference between the readings of the two groups was too slight to be of statistical significance except that the spinal anesthesia group showed definitely less decrease in per cent cholesterol esters on the third postoperative day ( $P=0.008$ ) and probably less on the seventh postoperative day

*Miscellaneous metabolic tests*—Studies on the excretion of 17-ketosteroids were made on Groups II, III and V of the herniotomy series There was considerable individual variation and a wide daily fluctuation Changes of statistical significance occurred, but they appeared to have little if any clinical significance Thus Group V showed a definite decrease on the day of operation and on the first postoperative day ( $P=0.0005$  and  $P=0.0168$ , respectively) The significance of the difference disappeared by the second postoperative day On the other hand, in Group III, which received daily intramuscular injections of 10 mg testosterone propionate in oil, there was no true difference between the preoperative value and that on the day of operation

Studies were made in creatinine excretion in groups I, II, III and V of the herniotomy series Differences of statistical significance were revealed but no clinical value could be attributed to the results except that the preoperative excretion in Group III, which received large quantities of protein, is definitely higher than in Group I, and insignificantly higher than in Group II In all groups except Group III the postoperative excretion was decreased compared to the preoperative level, but only on the day of surgery and the first postoperative day

In Groups II, IV and V of the herniotomy series, studies were carried out on *creatinine excretion*. No changes of statistical significance were detected except for an increase in the creatinine coefficients in Group III on the first postoperative day.

**TESTS FOR CIRCULATORY EFFICIENCY AND MUSCULAR FITNESS**—In this study of postoperative convalescence we have been limited in our choice of tests because many of them previously demonstrated by other investigation to be of value in studying convalescence were too strenuous to apply to patients with fresh operative wounds of the abdomen.

**Tilt-Table Test**—This test has been used by numerous investigators in studies on physical fitness and has yielded valuable information on the effect of posture (pooling of blood) on blood pressure and pulse. Since the test is designed to show the effect of blood pooling on blood pressure and pulse, it presumably should test primarily the efficiency of circulatory functions. A new method of converting the readings obtained into one score for the patient will be published elsewhere. Conversion of the numerous readings into one score was essential if patients in one group are to be compared to patients in another group.

In the herniotomy patients, the three groups which were ambulated (Groups VI, III and XII) had the best tilt-table scores (see Table I) having a rank of 1, 2 and 3 respectively in the 11 groups having tilt-table tests. The beneficial effect of ambulation can be proved by comparison of the three groups mentioned with other groups not receiving ambulation or with other groups not receiving ambulation but receiving more calories. For example Group VII (not ambulated) received more food than Group VI (during the first 4 postoperative days only) but had a tilt-table rank of 5 compared to a rank of 1 for Group VI which was ambulated. Group XI which was not ambulated had a tilt-table rank of 4, compared to a rank of 3 for group XII which was ambulated, except for ambulation, treatment was identical in these two groups.

In the patients having cholecystectomy, there was no significant difference between the two groups (XV and XVI) which differed only in the fact that ether anesthesia was used in one group and spinal in the other.

**Modified flammeter and Flack Test**—With few exceptions, the systolic blood pressure preoperatively dropped 10 to 20 mm after 25 seconds of blowing against a pressure of 20 or 30 mm of mercury, but at the end of the blowing period there was a sharp rise in pressure varying from 38 to 73 mm. The rise was greater when the patient was blowing against 30 mm mercury, and when he was tested in a tilted position (i.e. on the tilt-table).

As in most other tests, the postoperative performance was compared to results obtained preoperatively.

In 15 patients tested the reaction following blowing against 20 mm of mercury in the horizontal position had returned to normal in only one patient by the 3rd postoperative day. All patients in this category showed a normal response by the 8th or 10th day.

Six patients were tested in the tilted position, blowing against 20 mm of mercury. On the 3rd postoperative day the readings were normal on none of the patients. By the 10th postoperative day the readings on five had returned to normal, the response in one patient remained abnormal until the 20th day.

The response to blowing against 30 mm of mercury was similar to that just described except that some of the patients were unable to perform the test on the 3rd postoperative day. The delay in return to normal was slightly greater in this group, by the 11th day the response in two was still abnormal.

**Push-up test**—This test was used in four groups of patients having herniotomy. There was a remarkable consistency in the pulse rate 5 to 35 seconds and 60 to 90 seconds after termination of the test in all groups preoperatively, the pulse rate was elevated 19 and 11 or 12 beats per minute in the two periods respectively (See Table VIII). Postoperatively there was fair uniformity in Groups XII, VI and III, all of which were ambulated, the smallest increase in pulse rate was noted in Group XII which was ambulated and received a diet in which 40 per cent of the calories were derived from

TABLE VIII

Push-Up Test The Per Minute Difference Between the Resting (Recumbent) Pulse Rate at 5 to 35 Seconds and 60 to 90 Seconds After the Test The Test Required the Patient to Elevate Weights of 40 Pounds a Distance of 1 Foot 30 Times Per Minute for 2 Minutes All Groups Listed Are in Patients Having Herniotomy

Postoperative Average

Number	Management	Preoperative Average			1st Day			2nd Day		
		Resting Pulse Rate	5-35 Seconds	60-90 Seconds	Resting Pulse Rate	5-35 Seconds	60-90 Seconds	Resting Pulse Rate	5-35 Seconds	60-90 Seconds
\II	B+20% 40% protein tube fed ambulation	66	+19	+12	87	+14	+ 7	76	+15	+ 6
VI	B+20% 15% protein ambulation	63	+19	+12	68	+18	+ 7	66	+18	+ 9
III	Shot-Gun B+100%, 20% protein tube fed supplements and ambulation	78	+19	+11	98	+19	+13	93	+13	+ 8
V	B+20% 15% protein spinal anesthesia, no ambulation but mild exercise with certain tests	70	+19	+11	74	+28	+19	67	+29	+15

protein In Group V which was not ambulated, the average rise in pulse rate on the first postoperative day was 28 and 19 for the two periods compared to 19 and 11 for the preoperative figures These data show a tendency toward a greater degree of tachycardia following exercise with the push-up test, when the patient was not ambulated, and received a low protein diet The test was not used with patients with cholecystectomy

In the push-up test as well as several others herein described, we are relying upon the response of the heart rate to exercise as being an index of physical fitness Taylor and Brozek<sup>15</sup> remark that "the heart rate after a standard amount of work is probably the most useful single criterion of fitness in the study of convalescence" Unfortunately we know little about the physiologic mechanisms giving rise to the increase in pulse rate, but until these factors are known valuable data may nevertheless be discovered concerning methods of measuring and improving physical fitness

*Stair Climbing Test*—This test was used in three groups of patients with herniotomy, namely XII, VI and XIII as indicated in Table IX As might be expected, the results were similar to those obtained in the push-up test The best results were obtained in the group of patients with ambulation, and 40 per cent protein in their diet The poorest results were obtained in the non-ambulated group which had only 10 per cent of their calories from protein, although the total calories represented basal diet plus 100 per cent

TABLE IX

Stair Climbing Test The Per Minute Differences Between Resting (Sitting) Pulse Rate and the Pulse Rate at 5 to 35 Seconds and 60 to 90 Seconds After Test The test Required The Patients to Climb Two Flights of Stairs (44 Steps 6 $\frac{1}{4}$  Inches Each) in 35 Seconds

Postoperative Average

Group Number	Management	Preoperative Average			2nd Day			3rd Day		
		Resting Pulse Rate	5-35 Seconds	60-90 Seconds	Resting Pulse Rate	5-35 Seconds	60-90 Seconds	Resting Pulse Rate	5-35 Seconds	60-90 Seconds
XII	B+20% 40% protein tube fed Ambulation	77	+25	-2	90	+23	-3	82	+23	-9
VI	B+20% 15% protein ambulation	76	+33	+5	87	+42	+ 7	81	+38	+1
\XIII	B+100% 10% protein, no ambulation except with test	90	+28	0	103	+33	+ 6	96	+33	+7

Minus indicates less than resting

*Step-up Test*—This test is not considered satisfactory for use in postoperative convalescence because of the severe strain inflicted on an abdominal wound by rapidly stepping up and down. However, it was used in three groups of patients having herniotomy, although the test was not used postoperatively until the 7th or 11th day. The control group (non-ambulated basal diet plus 20, 15 per cent protein) showed a greater increase in pulse rate than the shot-gun group (ambulation, supplements, basal diet plus 100 per cent, 20 per cent protein), it showed a less pronounced increase in pulse rate than the group having basal diet plus 20 per cent, 15 per cent protein, spinal anesthesia and only slight ambulation.

*Change in Body Weight*—It is agreed that change in body weight is a very crude expression of physical condition, but the degree of shift in either direction may be a fairly accurate index of the efficiency of a certain regime when other factors remain constant. Unfortunately, the weight figures for our control group (II) are not available but Group IV is identical except that spinal anesthesia was used instead of ether. The weight loss in this group was 0.338 kg per day for the 6 postoperative days, representing the greatest weight loss of all groups studied. (See Table X) The smallest weight

TABLE X

Average Weight Loss From Day of Operation to Day of Discharge From Hospital (6 to 8 Days)

Group Number	Management	Average Daily Weight Loss (Kg)
III	'Shot-Gun basal diet +100% 20% protein Supplements Ambulation	0.033
VI	Basal diet +20% 15% protein ambulation	0.126
XII	Basal diet +20% 40% protein Tube fed Ambulation	0.133
VII	Basal diet +20% 15% protein Tube fed	0.185
VIII	Basal diet +20% 15% protein supplementation	0.227
XI	Basal diet +20% 40% protein tube fed	0.306
IV	Basal diet +20% 15% protein Spinal anesthesia	0.338

loss was 0.033 kg per day, occurring in the shot-gun group (basal diet plus 100 per cent 20 per cent protein, supplements and ambulation), which received high caloric intake and ambulation.

Groups XI and XII received the same treatment throughout except that the latter group was ambulated and the former was not, the weight loss in the ambulated group averaged only 0.133 kg per day whereas the loss in the non-ambulated group was 0.306 kg per day. Some of the other comparisons in Table X are not quite so decisive; but there is little doubt but what ambulation minimizes weight loss postoperatively.

*Miscellaneous Tests for Circulatory Efficiency or Physical Fitness*—*Vital Capacity* was determined preoperatively and on the 7th and 11th postoperative days in three groups of patients having herniotomy but no significant difference was detected in the preoperative and postoperative figures. The *Strength of Hand Grip and Endurance Time* using the Smedley dynamometer was performed in several groups of patients having herniotomy but no significant difference was detected preoperatively and postoperatively, in patients with cholecystectomy there was a slight decrement in strength of hand grip and endurance, but it was so slight that the test was considered of little value. The unmodified *Flameter test* revealed little information except a poorer postoperative performance in the older patients and in several instances dizziness occurred which was not apparent preoperatively.

**PSYCHOMETER TEST**—Early in our investigation it became apparent that such tests as steadiness of hand, speed of tapping, simple choice reaction time and coordination time were of little or no value, consequently they were abandoned.

**RENAL TESTS**—Various renal tests, such as the phenolsulphonphthalein test, urea clearance, and specific gravity were conducted on numerous patients with herniotomy, but since they revealed very little difference between preoperative and postoperative findings, they were discontinued early, other tests might be of value.

EVALUATION OF PROTECTIVE MEASURES USED—*Effect of Ambulation*—Ambulation appears to have a definitely beneficial effect on the nitrogen balance as illustrated in Table V and previously discussed. For example, in two groups of patients having herniotomy who had the same diet (bare maintenance) and treatment except for ambulation, the group having ambulation had a smaller negative nitrogen balance than the group not ambulated. When the diet was increased and all other factors kept the same, the group of ambulated patients had a greater positive balance than the nonambulated group. However, ambulation is unable to maintain nitrogen balance if the dietary intake is lowered significantly. For example Groups VI (ambulation) and VII (no ambulation) were given a basal diet plus 20 per cent, with 15 per cent protein, the former was ambulated and the latter was not. The only difference in the dietary intake was during the first 4 postoperative days, during which time the ambulated group received only intravenous alimentation on the day of operation and 1/4, 1/2, 3/4 and 4/4 diet during 4 postoperative days respectively, whereas the nonambulated group received a full dietary intake (by tube) each day. The negative balance was 13.8 Gm for the 6-day period in the nonambulated group (VII) compared to 21.3 Gm in the ambulated group (VI), thus indicating the importance of adequate food. (See Table V)

As indicated in Table I, the scores in the tilt-table test show a much better performance in the ambulated patients.

The results of the push-up tests are also slightly suggestive that ambulation during postoperative convalescence improves the cardiac or cardio-muscular reserve. In this series (see Table III) the non-ambulated (modified ambulation) group showed a greater postoperative increase in pulse rate after exercise than did any of the other three groups which were ambulated.

Ambulation appears to exert a definite effect on conservation of weight postoperatively, particularly when food intake and protein content are adequate or nearly so. When the figures on effect of ambulation and other factors as related to weight loss are submitted to actual statistical analysis it appears that ambulation is more important than high intake of food or protein individually or collectively, in maintaining postoperative weight of patients having herniotomy. (See Table X)

Considering the arrangements of groups it is difficult to draw conclusions as to the effect of ambulation on liver function. However, it is obvious that the effect is not very significant, hepatic impairment may be slightly reduced. For example, Group VI and Group II (See Table I) were treated the same except that Group VI was ambulated. In this group the urobilinogen excretion was 61 per cent of normal compared to 60 per cent of normal in the non-ambulated group.

EFFECT OF TYPE OF ANESTHESIA—The amount of urobilinogen excreted postoperatively is definitely greater after ether anesthesia than after spinal. For example Group II (control) and Group IV had exactly the same treatment (see Table I) except that the former group had ether and the latter group had spinal anesthesia for their operation (herniotomy). In the control patients the average daily postoperative excretion had increased to a point where the preoperative level was only 60 per cent of the postoperative level, whereas the increase in excretion in the spinal group was definitely less, i.e. the preoperative level was 86 per cent of the postoperative level. Group V was treated the same as Group IV except that the former had modified ambulation. There was no increase postoperatively in this group (IV) over the preoperative level, indicating that spinal anesthesia and modified ambulation together had completely abolished the decrement in liver function.

However a study of figures on bromsulphalein excretion, nitrogen balance and tilt table response reveals no significant difference in the effect of ether anesthesia as compared to spinal in herniotomies.

In cholecystectomy the hepatic impairment after operation was greater than after herniotomy but the difference between patients having ether and those having spinal anesthesia was not of statistical significance.

EFFECT OF HIGH PROTEIN DIET—Group VII and Group XI are suitable for this study in so far as all factors were the same except that the diet in the former group contained 15 per cent protein compared to 40 per cent in the latter. Judged by the urobilinogen test, the postoperative hepatic insufficiency was significantly less in patients receiving high protein diet. From the standpoint of figures alone (Table I) the bromsulphalein test indicates less hepatic insufficiency in the group of patients having only 15 per cent protein, however, when the figures are subjected to statistical analysis no significant difference can be demonstrated. The push-up test and the stair-climbing test (particularly the latter) show a distinctly better performance in the patients with 40 per cent intake of protein (Group XII) compared to that in patients with 15 per cent protein intake (Group VI). However, there is a second difference in the treatment of the two groups, namely, the fact that the patients with high protein intake also had maintenance of full diet during the first 4 postoperative days, whereas the patients with 15 per cent protein had no tube feeding on the day of operation, and  $1/4$ ,  $1/2$  and  $3/4$  diet for the first 3 postoperative days respectively. However, it should be stated that after several days all groups are back to normal.

There was a positive nitrogen balance of 9.6 Gm (for a 6-day period) in patients receiving a diet with 40 per cent protein compared to a loss of 13.6 Gm in the patients receiving a diet with 15 per cent protein. The tilt-table test revealed no significant difference between the two groups.

EFFECT OF HIGH CALORIC INTAKE—To determine the efficiency of high caloric intake in elimination of decrements, postoperatively, the best comparison is between Groups VII and XIII, since both groups were tube fed a diet containing the same number of grams of protein per gram of body weight, the difference in the treatment of the two groups is the fact that the total dietary intake in Group VII was basal plus 20 per cent, compared to a diet equal to basal plus 100 per cent in XIII, the increase in calories in Group XIII was derived solely from carbohydrates and fat. The performance of the patients in Group XIII was inferior to that of Group VII in all of the four major tests (See Table I). This indicates that a food intake as high as 100 per cent above basal requirements is distinctly detrimental, at least if the actual amount of protein per kg of body weight remains the same. We have no explanation for this phenomenon except that the increase in amount of fat might be considered very deleterious. Other experiments indicate that if the percentage of protein is increased, performance is improved by increasing caloric intake.

EFFECT OF MAINTAINING FULL DIET DURING THE EARLY POSTOPERATIVE PERIOD—Since the conventional dietary management of patients with abdominal operations consists of no oral feeding on the day of operation and perhaps  $1/4$ ,  $2/4$ ,  $3/4$  and  $4/4$  diet for the first 4 postoperative days respectively, we conducted numerous experiments with this diet, comparing results with patients having a full diet (by tube) during this period.

A comparison between Group VII and Group II yields data on the value of full diet during the early postoperative period since each group had the same treatment and diet (basal plus 20 per cent, 15 per cent protein) except that the former group had a full diet during the first 4 postoperative days whereas the latter had no oral intake the day of operation and  $1/4$ ,  $1/2$  and  $3/4$  of full diet, respectively, during the first 3 postoperative days. The patients having full diet during this postoperative period had a better performance score with all 4 tests. The marked difference between the final rank (5 compared to 11) of the two groups can be explained only by one factor, namely, the difference in dietary intake during the day of operation and the first 3 postoperative days. The importance of a basal caloric intake during the early postoperative period is thereby strongly emphasized.

#### SUMMARY

We have conducted numerous physiologic tests on 92 patients having herniotomy and 10 patients having cholecystectomy. Of eight or nine liver

function tests studied, the urobilinogen and bromsulphalein tests were found the most valuable, at least in our studies. Practically all patients showed impairment of liver function for two to five days following operation, this decrement was greater in the cholecystectomy patients than in the herniotomy patients, it was increased considerably by numerous complications (See Table II). The impairment was less after spinal anesthesia than after ether. In general, this impairment could be prevented by a high protein diet or ambulation (except in the presence of complications).

Studies on nitrogen balance revealed a negative balance postoperatively except when the diet was increased to a level (with increased protein content) above the average postoperative diet. Ambulation had a distinct sparing effect on nitrogen but an increase in the protein content above a 15 per cent level was necessary before a positive nitrogen balance was achieved. Spinal anesthesia had no sparing effect on nitrogen, but in the urobilinogen test showed less hepatic impairment after spinal than after ether anesthesia.

Serum total proteins showed no significant change after herniotomy, but after cholecystectomy there was a definite decline in the serum albumin which was maximum on the 11th day.

There was a definite decrease in the cholesterol and cholesterol esters in the cholecystectomy group, but the decline was too slight in the patients with herniotomy to be of statistical significance except on the third postoperative day.

The tilt-table test was considered to be of definite value in estimating speed of convalescence. The tilt-table scores were much improved by ambulation. Diet appeared to have less effect although patients with a diet of basal plus 20 per cent with 40 per cent protein had a better score than patients with a diet of basal plus 100 per cent with 15 per cent protein.

Preliminary experiences with a test combining and modifying the flammeter and Flack test are very encouraging, particularly since the test is a simple one requiring very little time and experience on the part of the operator. During the period of blowing, the pulse rate is elevated and the blood pressure decreased, immediately after the test, the blood pressure rises sharply for a very short time. With this test normal response was not regained before the 10th or 12th day.

In the push-up test (performed on herniotomy patients only) the best scores were made in two groups which were ambulated, one having a diet consisting of basal plus 20 per cent with 40 per cent protein and the second having a diet consisting of basal plus 20 per cent with 15 per cent protein (Table VIII). A third group which likewise was ambulated had an inferior score presumably because of a high food intake and supplements.

In the stair-climbing test the best scores were obtained in the group of patients with basal diet plus 20 per cent, with 40 per cent protein, and ambulation (Table IX). The score was not as good when the protein content was decreased to 15 per cent even though the caloric intake was the same and the patients were also ambulated. The score of the non-ambulated group was

still lower, even though a diet of basal plus 100 per cent (with 10 per cent protein) was given

Certain conclusions about dietary intake can be drawn. In general, the best performances were obtained when a high protein diet was given. A high caloric intake itself did not improve the test performances, in fact, it appeared distinctly to be detrimental to performance. When a full diet is given every day postoperatively, performance scores are better than when the conventional diet of  $\frac{1}{4}$ ,  $\frac{1}{2}$ ,  $\frac{3}{4}$  and  $\frac{1}{4}$  dietary intake is given during the first four post-operative days respectively.

In general, ambulation had a beneficial effect on the scores of all tests, except the urobilinogen test, which alone revealed no difference between ambulated and non-ambulated patients.

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DISCUSSION—DR CHARLES C. LUND, Boston. In the first place, Doctor Cole should be congratulated on the tremendous amount of hard work that has gone into this study. Anyone who has had experience with metabolic studies in patients has a great admiration



for one who can run such studies in so large a group I had the good fortune to see the manuscript that Doctor Cole summarized at this meeting, and had the opportunity to study it at my leisure. He has covered so much ground in a few minutes that I am going to emphasize some of the points.

In the first place, he speaks of a "shotgun" complete diet. His paper lists a long list of supplements, all the well-known vitamins in large doses, starting with K and C, riboflavin, and so on, down to some of the cruder forms like liver extract and some of the amino acids considered important in metabolic work. The last table he presented was concerned with weight loss. Many surgeons do not take much consideration of any metabolic upset if relatively slight, but these hernia patients were protected by probably a better than average hospital diet and the loss of weight, while not spectacular, was real. It amounted to six or seven pounds loss in a week, with or without ambulation. When he gave a double diet and ambulation together, he essentially eliminated the loss.

This emphasizes the point Elman made in more serious operations, that there was a very serious metabolic upset.

I was surprised that he found as great a decrease in serum albumin following operation, as 25 per cent in patients under ether. With spinal anesthesia there is a loss, but not as much. Everything we can do to keep patients as nearly normal as possible at the time of operation and immediately afterward, is being shown by more and more investigators to be the proper attitude for the surgeon today.

DR WILDER PENFIELD, Montreal. I think what Doctor Cole said applies to many different types of surgery. My associate, Doctor Cone, and I have found it particularly important to get patients out of bed early after removal of intervertebral disks, because it seems to promote fusion or fixation of the two vertebrae. Weight upon the vertebral column obliterates the intervertebral space.

I should like to ask Doctor Cole a question in regard to terminology, particularly as I know him to be a scholar as well as a scientist. The question refers to the term ambulation. For a new conception it is often wise to employ a new or little used word. But he should indicate to us its correct usage. The verb ambulate, for example—is it intransitive, or does the doctor ambulate the patient? Is it correct to make it an adjective and speak of the ambulated patient?

DR FRASER N. GURD, Philadelphia. Doctor Cole was kind enough to give me access to his material yesterday. When I told my chief, Doctor Ravdin, that I considered it a significant contribution, he suggested that I step up here and say so, which it is my pleasure to do. The work of Doctor Cole and his associates is closely related to that being done at present, under Doctor Ravdin at the University of Pennsylvania, on the factors affecting the regeneration of liver substance. There can be little doubt that the absolute protein content of the liver is the best measure available of effective liver size. On the relation of diet to the liver protein, Kosterlitz of Aberdeen has stated recently that the amount of cytoplasmic material present in the liver is directly proportional to the logarithm of the casein intake. Dr. Harry M. Vars and I have done some work on this facet of the problem of liver regeneration.

We have prepared rats for 14 days on a protein-free diet, then subjected them to 70 per cent hepatectomy. In a standard recovery period we have measured the amount of new liver protein being formed and also the nitrogen balance. Postoperatively, we have fed a variety of diets, starting from the base line of a protein-free diet both before and after operation. A certain important amount of liver protein is restored even on a protein-free diet, and this amount appears irreducible by any degree of dietary restriction including complete starvation. We have added to the postoperative diets casein at varied levels and other proteins of different biologic values. With dietary protein added, the basal regeneration obtained on the protein-free diet is sharply increased. We have found the closest correlation between the amount of new liver protein formed and the net nitrogen balance. That is to say, those animals eating the smallest amounts of useful protein, and

exhibiting an unfavorable nitrogen balance, have shown relatively little liver protein regeneration. But by increasing the dietary protein, in proportion to the degree to which the nitrogen balance was strengthened, so has the liver protein been restored. One must emphasize the nitrogen balance rather than the nitrogen intake, because we have shown that the ingested protein favors liver recovery only to the extent to which it remains in the body. The nitrogen balance is the resultant of many influences which are difficult to control independently, but which Doctor Cole has attempted to control. Among such influences are many dietary and environmental factors, stresses like infection, and perhaps the elimination of total physical disuse by getting patients out of bed.

Although it will be extremely difficult to prove such a thesis in the human, I feel that what Doctor Cole is probably measuring is the absolute amount of functional liver cytoplasm. We have definite quantitative measurements of it in the rat, but until we know of a way to measure the total mass of the liver *in vivo* in the human, we are obliged to estimate it by indirect measurements such as Doctor Cole has brought forward.

DR WARREN H. COLE, Chicago (closing). First I want to thank Doctors Lund, Penfield and Gurd for the very interesting points they brought up in their discussion. From two viewpoints I am much interested in the point which our worthy English scholar, Doctor Penfield, brought up regarding the definition of ambulation. True enough, the meaning of ambulation is extremely varied in the minds of many people. Some doctors are of the erroneous opinion that if the patient is sitting up on the side of the bed he is being ambulated, but he is not, a patient may easily develop a thrombus of the veins of the leg while sitting in this position. The patient must walk about. In our ambulation regime we have added exercises which involve practically all the muscles of the body. I do not consider sitting in a chair to be part of ambulation. Regarding the second part of Doctor Penfield's question—when can ambulation be used as a noun, verb, adjective, etc.? The dictionary allows us considerable liberty in that respect, but if enough people continuously use a certain word not in the dictionary, it will finally be placed in Mr Webster's dictionary. In other words, usage constitutes law in that respect.

I heard someone ask about patients climbing stairs on the first or second day post-operatively. Obviously, while patients are doing this someone must accompany them. Some of these patients were on the ambulation regime, being given extensive exercises. Others were given no exercises and were kept in bed except during tests, they were classified as non-ambulatory although they did receive some exercise in their test. We did not use the step-up tests of the Harvard type. Although the step-up test is a fairly good test for determining rate of convalescence, I am firmly of the belief that it is too strenuous to use in the first few days after a major operation.

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## ERRATUM

In the announcement concerning the Editorial Board of ANNALS OF SURGERY in the July issue, the biographical note for Dr Michael E DeBakey was regrettably in error. We would much appreciate your noting that Dr DeBakey's title is that of Associate Professor of Surgery at Tulane University School of Medicine rather than Assistant Professor, as stated.

# REPAIR OF SLIDING INGUINAL HERNIA THROUGH THE ABDOMINAL (LAROCQUE) APPROACH\*

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THIS PAPER IS INTENDED to emphasize the advantages of the abdominal approach to the sac and bowel in sliding hernia of the colon. The same mechanism is involved in hernia of the tube and ovary in the female, and the abdominal approach to these organs has the same advantages. Williams<sup>1</sup> Hernia of the bladder, however, while usually classed as a sliding hernia is involved in direct inguinal hernia and can be handled better from below.

There is still confusion in the minds of many young surgeons and not a few older ones concerning the exact nature of sliding hernia of the colon, this is true in spite of the accurate descriptions of this condition which have been in the literature for many years.

The earliest description of a sliding hernia of the colon which I have found is by Percival Pott<sup>2</sup> in a chapter on Incarcerated Hernia from his Treatise on Hernia published in 1783. He gives a long and involved description, which undoubtedly was of this condition, though it lacked the concise accuracy of his slightly later colleagues. He was in no way lacking in directness, however, when, expressing his opinion of those who operated on this type of hernia, he said "But I also know that such accidental successes have emboldened the same operators to commit more than one or two murders in similar cases, and that, from the prevalence of the fashion, some of these rupture-doctors have been largely rewarded, when they ought to have been hanged."

Rutherford<sup>3</sup> quotes Scarpa in a good description from his book published in Milan in 1809. Three eminent European surgeons of a slightly later date understood and described this hernia well. Hesselbach was quoted by Samuel Cooper<sup>4</sup> in 1841. "When in these ruptures of the right side, the cecum, or, in those of the left, the colon, are met with closely adherent to the hinder side of the hernial sac, the adhesion is not to be looked upon as the effect of disease, since it is the perfectly natural connection of those bowels with the peritoneum. On the left side the parts most commonly protruded are the colon and omentum." Liston<sup>5</sup> in the American Edition of his surgery published in 1838 says "Sometimes the fixed portions of the colon slip down, their posterior cellular attachments behind being carried into the inguinal canal, a peritoneal sac invests the anterior aspect only." Sir Astley Cooper<sup>6</sup> in his Lectures published in Philadelphia in 1839 gave as one of the causes of irreducible hernia, "A protruded cecum, in which the intestine adheres by cellular membrane

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\* Read before the American Surgical Association at Hot Springs, Virginia, March 26, 1947

## SLIDING HERNIA

behind, and the sac exists only on the fore part" He had given these lectures for more than 30 years before their publication so he may have been the first to understand and describe this hernia

Perhaps the reason that sliding hernia is generally so poorly understood is that it is relatively rare The incidence related to all hernias is about 15 per cent, it has been variously reported from 1 per cent to 3 per cent

The vast majority of reports indicate that the hernia is usually repaired through the inguinal approach All authors agree that accurate diagnosis

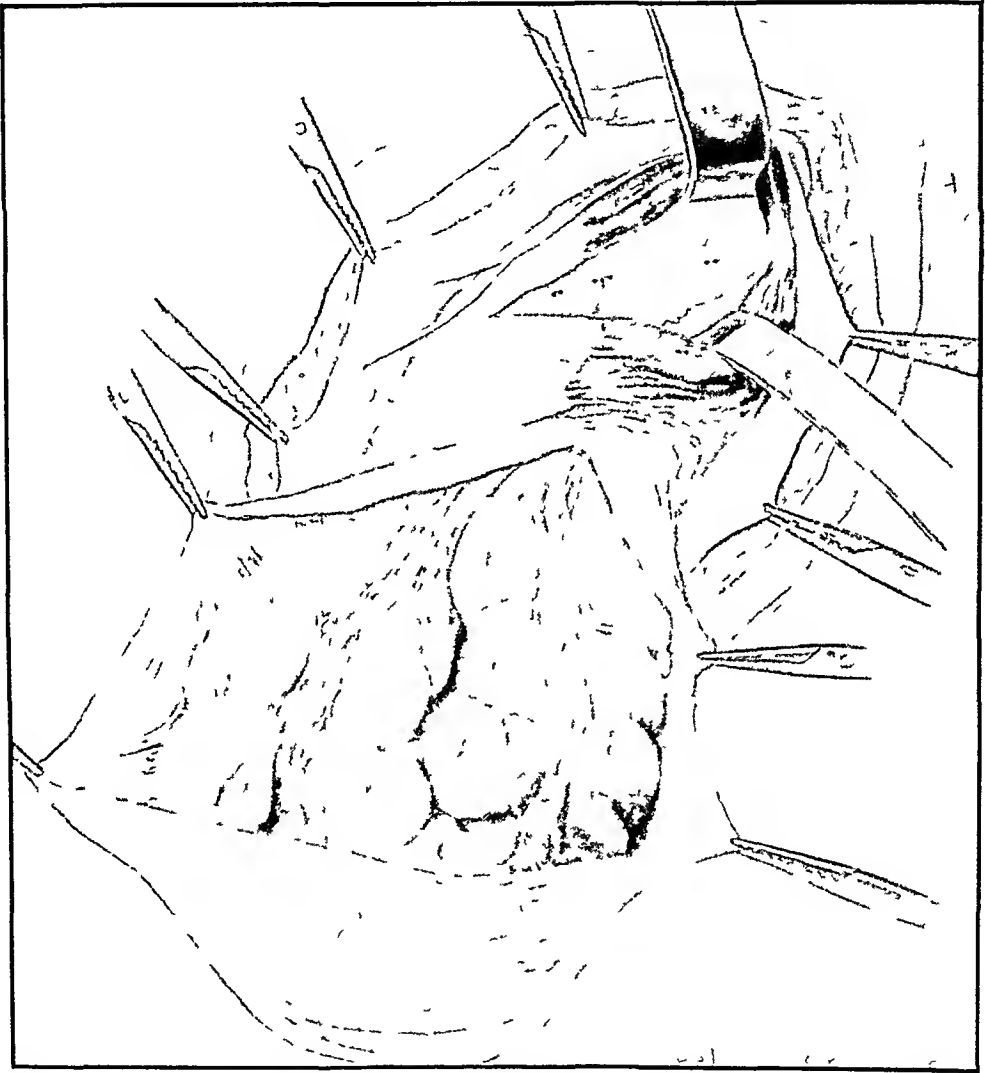


FIG 1—Sac open showing sliding colon, muscle splitting incision has been made above internal ring

cannot be made until the sac is exposed and often not until the sac is opened It should be suspected when the hernia is indirect, difficult or impossible to reduce completely, difficult or impossible to control by pressure, and has a large defect at the internal ring Positive diagnosis can sometimes be made by x-ray examination after Barium Enema Lyons, Brogan, and Sawyer<sup>7</sup>

The dissection of the sac and colon is attended by some danger of damage to the blood supply of the cecum or colon particularly when the nature of the

hernia is poorly understood by the operator. Demel<sup>8</sup> reports a mortality of 28 per cent of 501 collected cases, the deaths occurred when the colon was resected. Moschowitz,<sup>9</sup> Lamson<sup>10</sup> and others also called attention to the danger of injury to the wall of the bowel or its blood supply. Reports of operations on sliding hernia were made 100 years ago but of the modern authors the operation of Weil<sup>11</sup> began the reconstruction of the mesocolon. He made

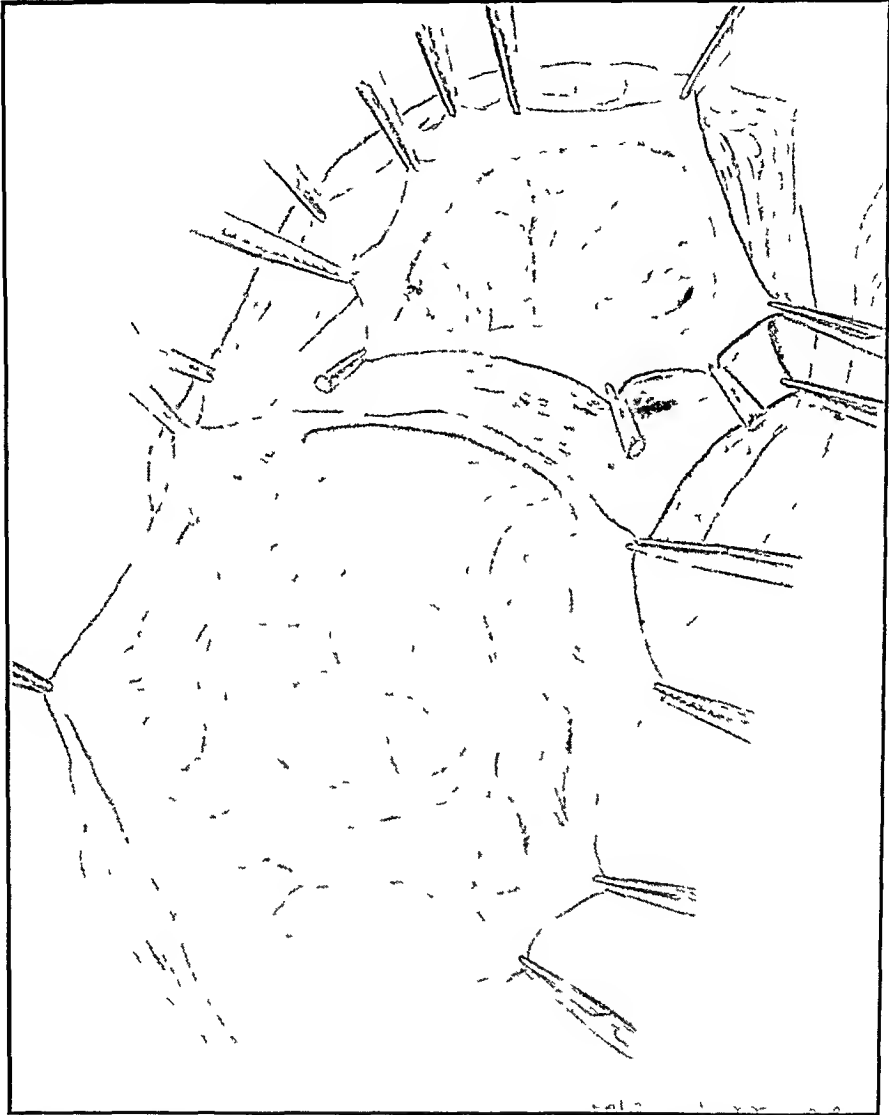


FIG 2—Peritoneum open showing colon on left side entering the internal ring

flaps of the sac and sutured these flaps behind the mobilized bowel, he then closed the reconstructed sac. Hotchkiss<sup>12</sup> did much the same except that he cut away the excess of sac before he sutured the edges to construct the mesocolon. These methods have been modified by Kirchner,<sup>13</sup> Walton,<sup>14</sup> Bevan,<sup>15</sup> and Burton and Blotner.<sup>16</sup> All of these methods of constructing a mesocolon are

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considered dangerous by Culey<sup>17</sup> on account of possible constriction of the blood supply. He pushes the bowel upward into the abdominal cavity, removes the excess of sac and sutures it. Zimmerman and Loufman<sup>18</sup> do much the same except that they close the sac as high up as possible before dissecting the bowel posteriorly. David<sup>19</sup> introduced another modification in three cases of congenital hernia associated with sliding of the cecum. He divided the sac

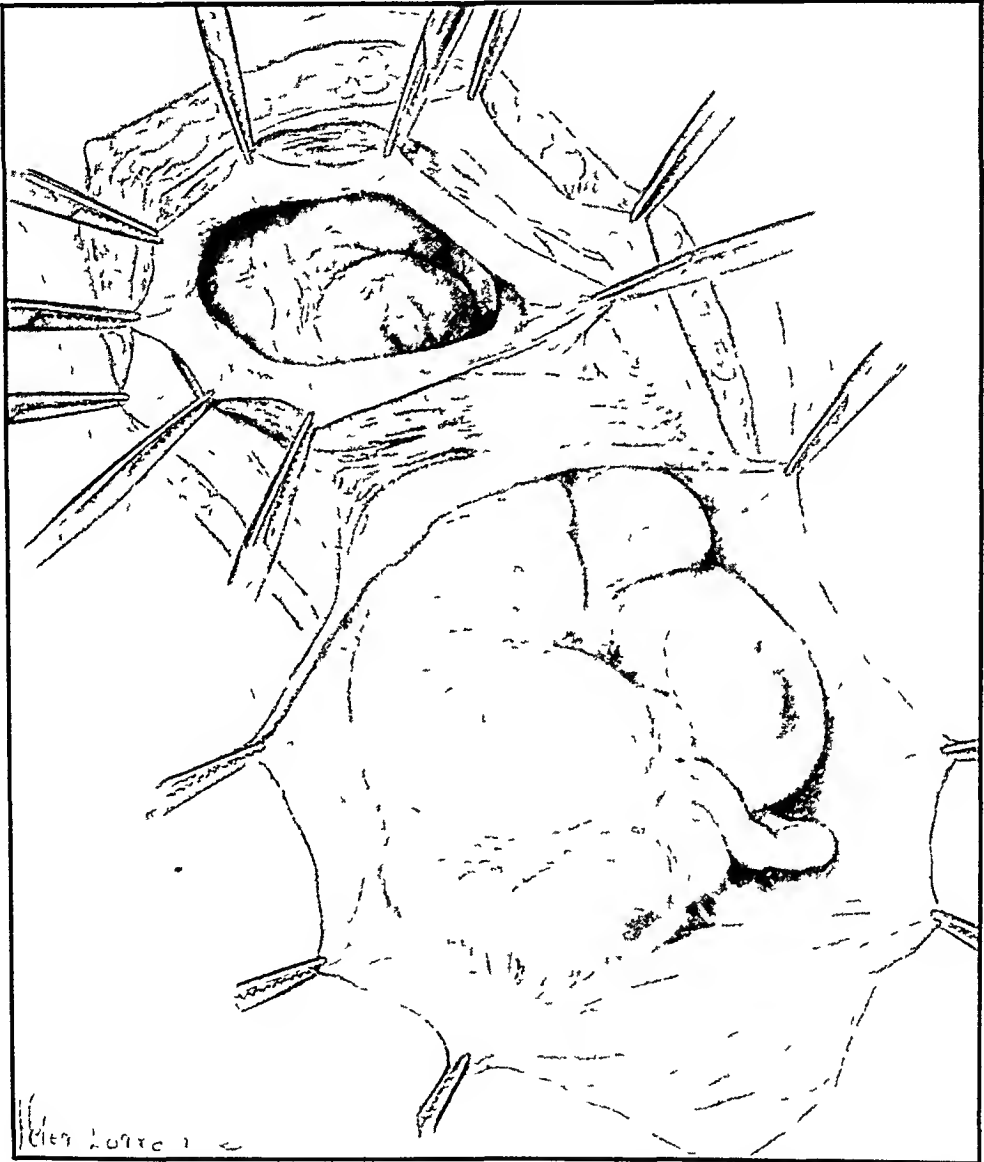


FIG 3—Peritoneum open showing cecum on right side entering the internal ring

transversely above the testicle, then incised the upper portion longitudinally on each side of the cecum and when the cecum had been returned to the abdomen, sutured the anterior flap behind it.

The slide of the colon probably results from the pull of the complete portion of the sac which doubtless exists before the colon descends and also from the pushing of increased abdominal pressure. The descent is made possible

by a large internal ring and in adults the presence of excess fat is probably another factor

To accomplish complete reduction of this hernia, that is to replace the colon well into the abdominal cavity away from the internal ring and to completely remove the sac, it would seem logical to reverse both of the stress factors. All of the operations from below combat the pulling but do not correct the push from above. When we can lift the bowel upward through another opening we

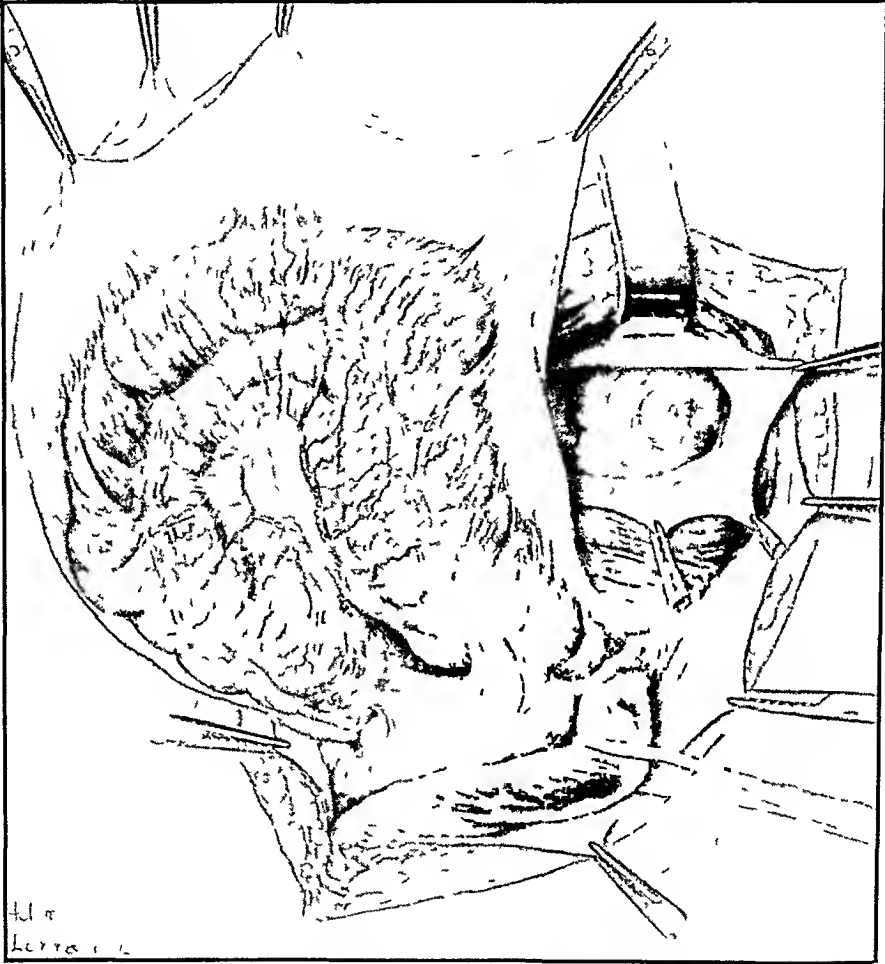


FIG. 4—The sac and colon have been dissected from the cord and lifted, showing the posterior surface of colon and its blood supply

accomplish both of these forces and in addition entirely remove the sac and the excess peritoneum. Complete repair of the internal ring is also improved.

The advocates of opening the abdomen above the inguinal canal may be divided into two groups: first those who make this opening for exposure in fixing the colon to the abdominal wall, after the hernia has been repaired in the canal, and second those who use the opening for reduction of the hernia and removal of the sac.

The first report of opening the abdomen above the inguinal canal was

made by Fiaschi<sup>20</sup> in 1907. He considered recurrence due to "the vicious habit of sliding down acquired by that portion of the intestine forming the sliding hernia." He advised a muscle-splitting incision for colopexy as a supplement to the repair from below.



FIG 5—The colon has been delivered into the upper wound

Robins<sup>21</sup> in 1909 reported the reduction of strangulated inguinal hernia through a rectus abdominal incision, this is probably the first use of the abdominal approach for the reduction of hernia and the removal or closure of the sac.



LaRoque<sup>22</sup> in 1919 advocated the approach through a muscle-splitting incision above the internal ring for all inguinal hernias. He elaborated his technic in 1924<sup>23</sup> and described in detail the application of this method to sliding hernia in 1932.<sup>24</sup> Williams<sup>1</sup> and Barnes<sup>25</sup> who had adopted this method from LaRoque later emphasized its advantages.

Moschowitz<sup>9</sup> in 1925 advised the use of a muscle-splitting incision for the reduction of small sliding hernias and a ventral incision for the large ones, but he closed the sac remaining in the inguinal canal from below.

Watson<sup>26</sup> in 1925 described the use of a ventral incision for colopexy and also advised its use for reduction of large sliding hernias.

Roscoe Graham<sup>27</sup> in 1935 reported the use of a rectus incision to reduce the hernia and to suture the mesocolon after dissection of the sac in the canal.

Mackid<sup>28</sup> in 1936 described essentially the same method but he overlapped the sac in restoring the mesocolon.

Brown<sup>29</sup> in 1943 reported satisfaction in using a technic almost identical with that of LaRoque.

Jacobson<sup>30</sup> in 1946 advised the use of this technic in all inguinal hernias.

The advantages of the abdominal approach and particularly the approach through a muscle-splitting incision above the internal ring are not generally appreciated. I have been surprised at the small number of my surgeon friends who use this method. It is indicated also by its complete absence in the text on sliding hernia in *Watson's Hernia*<sup>31</sup> (1938) and in the chapter on Hernia by Harvey Stone in Lewis & Walter's *Practice of Surgery*<sup>32</sup> (1941). In Johnson's *Operative Therapeutics*<sup>33</sup> (1915) a rectus incision for fixation of the colon is mentioned and in Horsley and Bigger's *Operative Surgery*<sup>34</sup> (1937) the LaRoque technic is described, but it is not applied to sliding hernia.

A query was sent recently to the members of this and the Southern Surgical Association concerning the use of the abdominal approach to the sac of sliding inguinal hernia. Two hundred forty replies were received, 69 used the abdominal approach, 15 occasionally used it, and 156 did not use it. It would, therefore, seem that the advantages of this technic are not generally recognized and that it would be worth while to present it again.

The usual inguinal incision is made, the external oblique is opened into the external ring, the sac is exposed and dissected from the cord, the sac is opened on its anterior surface and the sliding colon is exposed (Fig. 1). The internal oblique and transversus abdominis are then opened about 1 inch above the internal ring, with care to avoid the iliohypogastric nerve. There is often a fairly firm layer of transversalis fascia at this level which can be used later in the repair. The muscles are retracted and the peritoneum is opened transversely. The contents of the hernia are now revealed from above as they enter the internal ring. Figure 2 shows the double barrel descending or sigmoid colon on the left side and Figure 3 shows the cecum on the right side. The sac is now completely dissected from the cord and the colon is mobilized with care to avoid damage to its blood supply which lies posteriorly (Fig. 4). Traction on the colon from the abdomen draws it and the sac into the cavity.

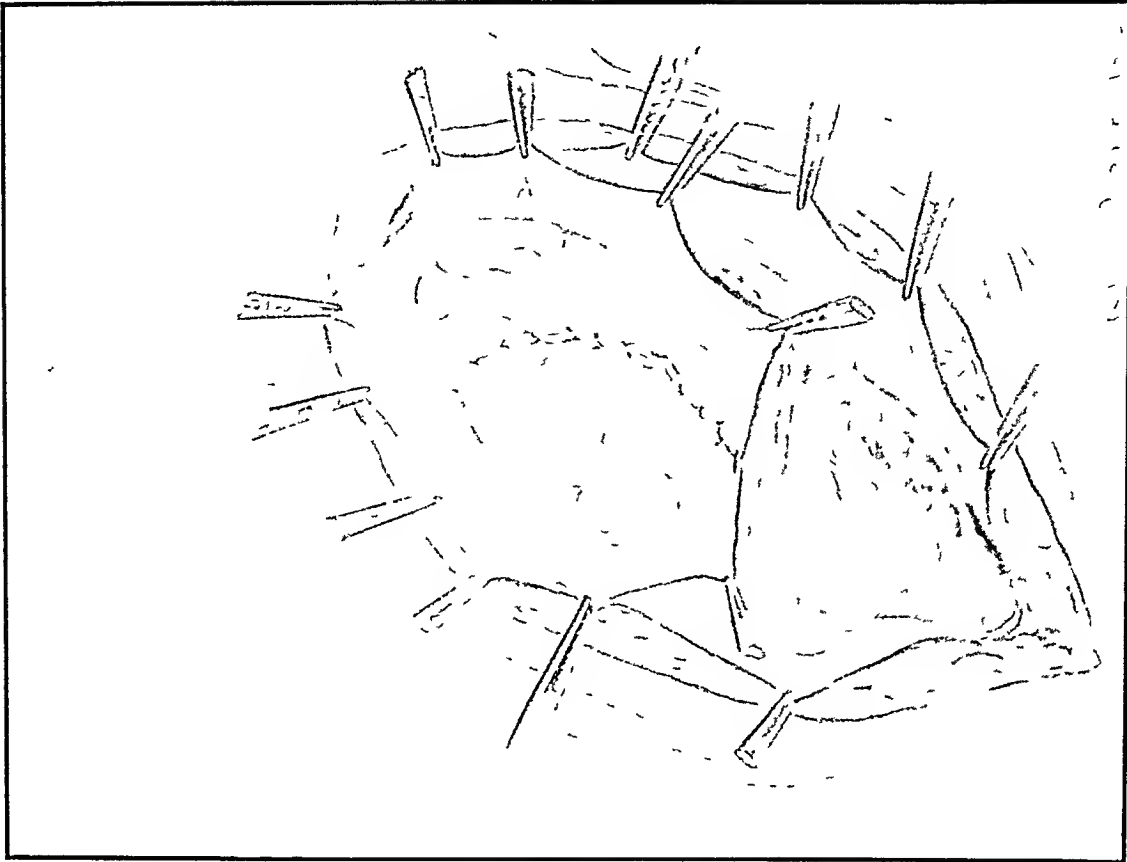


FIG 7—The colon has been restored to the abdominal cavity. Note the suture line in the mesocolon extends into the abdominal incision

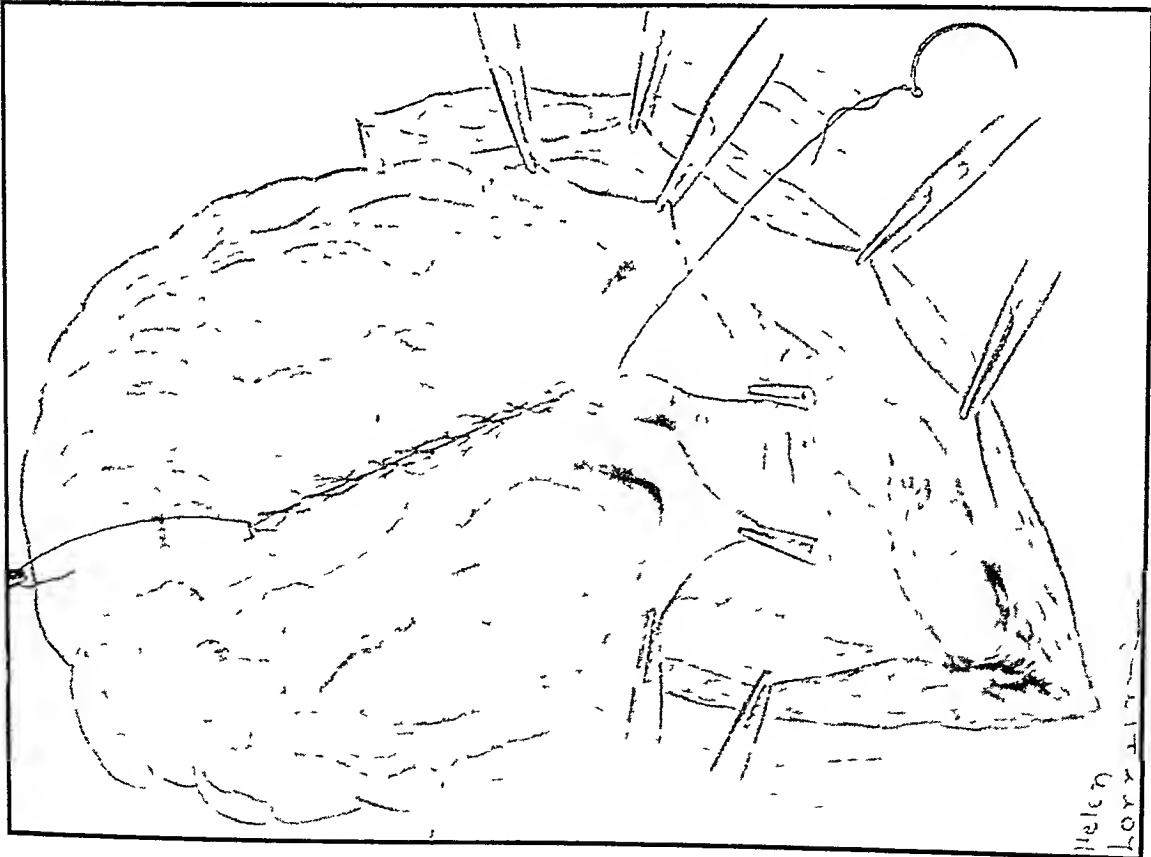


FIG 6—Excess peritoneum of sac has been removed, the mesocolon is being reconstructed

It is now obvious that the antero-lateral wall of the sac is the outer leaf of the mesocolon and is continuous with the lower lip of the upper opening into the peritoneal cavity—(Fig 5) The excess peritoneum is cut away, the mesocolon is closed by suture and the bowel is restored to the peritoneal cavity—(Figs 6 and 7) The peritoneum is now sutured—it should be noted that the suture line in the mesocolon runs into the lower lip of this incision—(Fig 8) When the transversalis fascia is present with sufficient strength it can be

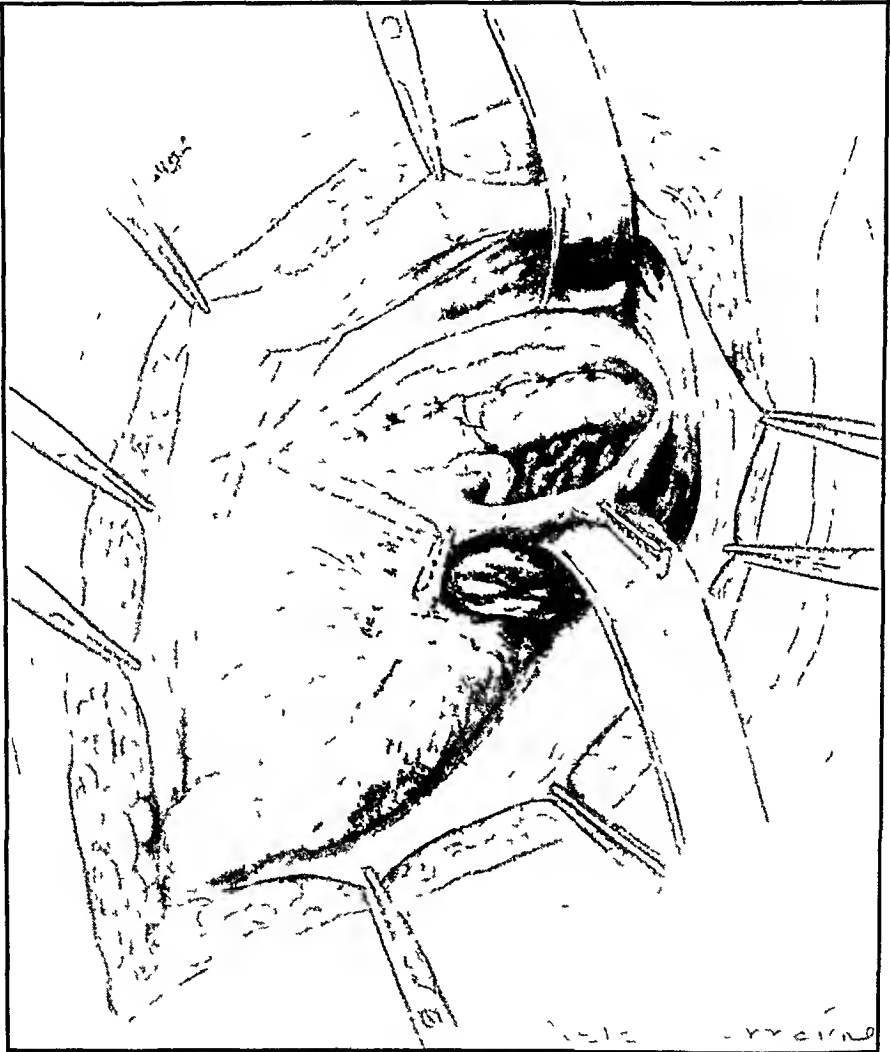


FIG 8—The peritoneum has been closed, the transversalis fascia is shown

sutured so as to make an extra support to the superior portion of the internal ring. The internal oblique and transversus abdominis are then sutured.

The operator now returns to the inguinal canal to make the repair as he may desire. It has been my practice to use the Bassini method, modified by the use of a fascial flap from the rectus sheath or a fascial strip suture from the upper margin of the divided external oblique aponeurosis according to the

size of the defect and the condition of the tissues available for the repair. It is particularly important to have a snug internal ring, some operators have advised complete division of the cord, and other excision of the testicle and cord (Gabb<sup>17</sup>). The former entails considerable risk of slough of the testicle which may endanger the whole repair, the latter is distasteful to the patient, and conditions which would demand either must be extremely rare.

The advantages of this procedure are

1 The dissection of the posterior portion of the colon can be completed from above where a better view may be had of the blood vessels to the colon, it is, therefore easier and safer.

2 The entire sac and excess of peritoneum is removed, this is difficult from below and it is the most important part of any operation for indirect hernia.

3 The mesocolon can be reconstructed in the anatomic position of the bowel.

4 Unusual conditions of the sac and its contents can be more readily recognized and repaired. Garlock<sup>16</sup>

5 The colon may be fixed to the abdominal wall if desired.

6 The muscle-splitting incision above the internal ring gives better access to the sac than the rectus incision, it is much more simple and easy, and it is adequate to handle the defect on either side of the body.

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DISCUSSION—DR ROSCOE R GRAHAM, Toronto We are indebted to Doctor Williams for bringing forward this problem of sliding hernia. One is amazed to find that in the reply to the questionnaire which Doctor Williams sent out, there was such a percentage of surgeons who did not use the transperitoneal approach in the repair of sliding hernia.

It is tremendously important that we stress the diagnostic points which are helpful in the preoperative recognition of a sliding hernia, particularly when we are so liberal in allowing the resident staff to operate upon herniae without strict supervision.

We should suspect the diagnosis of a sliding inguinal hernia when there is a history of a long-standing hernia, when a truss which formerly was efficient can no longer be worn because of pain and irritation, and finally the hernia becomes irreducible. Sliding hernia can be confirmed by a barium enema, showing large bowel in the sac. At operation the presence of a large mass, thick, and without a definite margin of a sac, puts one on guard. In our experience it has not been necessary to excise any peritoneum. A withdrawal of the sigmoid or cecum into the peritoneal cavity has shown that the peritoneum presenting in the inguinal canal is peritoneum covering the mesentery of the bowel, and it can be readily closed with a few sutures. The ease, safety and permanency with which one can deal with a sliding hernia by the peritoneal approach makes it undoubtedly the ideal technical procedure.

DR C REID EDWARDS, Baltimore I think Doctor Williams is to be complimented for calling attention to the abdominal approach to this type of hernia. It is a hernia that is turned over frequently to the house man for operation, and the senior man bears considerable responsibility. I am sure you all can recall the older textbooks in which a print of a scrotal hernia appeared, the title was "Scrotal hernia in which the abdominal contents have lost the right of domicile." On the left, the sliding hernia will have the sigmoid, on the right, the cecum and much of the ileum.

A few years ago a Negro was admitted to the hospital with a scrotal hernia descending to the knees. He had made a harness for himself. We thought it wise to investigate the sac before undertaking an operation, and we found the ileocecal valve at the upper level of the patella. That is an exaggerated case, but it shows what can happen in a neglected case. There is no use even thinking of the usual operative procedures. The contents of the abdomen have been out for too long, the viscera have sacrificed the "right of domicile." Any attempt to put that back is likely to damage the circulation to the right and left colon.

In a patient who is excessively fat, it is wise, after proper x-ray, to turn him over to the medical service for weight loss. This man lost 26 pounds and then came to operation. A long paramedian incision was made and it was not possible to pull the contents back into the abdomen. Then an inguinal incision was made, and it was still not possible. So then all structures were divided at the spine of the pubic bone, the entire wall was reflected and, with difficulty, the mass could be turned back into the peritoneal cavity and the structures apposed.

I believe it is wise to advocate study by x-ray of all gross sliding hernias, to establish definitely what part of the bowel has descended into the scrotum, and how much risk there will be of endangering the vascular supply to the colon

DR. WILLIAM L. ESTLS, JR., Bethlehem, Pa. I have been meeting the problem of the sliding hernia from a little different angle and have, therefore, been very much interested in Doctor Williams' presentation. We have been using for the correction of sliding and other hernias a so-called fascia-to-fascia rectus sheath closure. In this operation the sheath of the rectus is split about 1 cm. medial to the margin of the muscle, the entire length of the inguinal canal. This lateral margin of the rectus sheath is sutured with interrupted cotton sutures to Cooper's ligament as originally suggested by Harkins and McVey for the usual Bassini procedure. The second layer for the posterior wall of the canal is then formed by suturing the external oblique attached to Poupart's ligament to the medial margin of the sheath of the rectus, thus giving two layers of superimposed sutured fascia for closure of the posterior wall. The operation is completed by suturing the lateral margin of the external oblique muscle over the cord to Poupart's or the inguinal ligament.

However, an important part of the operation is the correction of any defect of the transversalis muscle before the above method of closure is begun. The defects usually found are orifices of direct herniae, a large internal ring, or a weakness of the muscle close to the pubic spine. These are closed by interrupted cotton sutures.

In the case of sliding hernias we rarely open the sac. The hernia is carefully freed from the structures of the cord and restored to the peritoneal cavity, and the large internal ring is closed with interrupted cotton sutures, the operation is concluded by the above fascia-to-fascia rectus sheath procedure. We have recently studied follow-up results covering three years or more. All patients have been examined personally. Of 119 indirect hernias there was one recurrence, in 56 direct hernias, three, and in 11 recurrent hernias, no recurrence. Of this entire group, 26 were sliding hernias with no recurrence. The over-all recurrence rate, therefore, was found to be 2.2 per cent.

There is, however, a definite possibility of atrophy of the testicle if the internal ring is closed too snugly. We have avoided this by not angulating the cord by suturing too high at the internal ring, and being careful to have an opening at the internal ring at least 1.5 cm. in diameter.

We therefore feel justified in suggesting this method of treatment as effective for sliding hernia, as well as the method Doctor Williams has described.

DR. CARRINGTON WILLIAMS, Richmond, Va. (closing). Doctor Graham and I are almost in entire accord on sliding hernias. I do think there is usually a small sac at the bottom of the mass. Doctor Edwards' large hernia was certainly unique, and proves that there are instances where the abdominal approach is very useful. Doctor Estes' report of non-recurrence is indicative of the fact that abdominal approach is unnecessary, perhaps the Estes repair shop in Bethlehem is better than mine in Richmond, because the only case of recurrence I had was one that looked so easy that I did not use the approach from above.

# REPAIR OF MAJOR FACIAL INJURIES\*

JAMES BARRETT BROWN, M D

St LOUIS, MISSOURI

AND

BRADFORD CANNON, M D

Boston, MASSACHUSETTS

SOME OF THE SALIENT PROBLEMS and some of the methods of repair in caring for patients with major facial injuries are presented here. Including the great numbers seen in military service, the most frequent causes are gunshot wounds, burns, traffic crashes, radiation exposure and freezing. (The defects of congenital origin and those resulting from cancer are of a group dealt with elsewhere.)

The surgeon like the tailor can make no better coat than his cloth and it is well to realize limitations as well as possibilities in attempting major repairs. There is only one original and most surgical restorations are only substitution. Diagnosis is of major importance and includes determination of what tissue has been lost or displaced as well as what distorted function to expect from it.

One often has to hold in abeyance rules that are promulgated for general usage over the body—such as the cutting debridement or packing all wounds open. These two measures were aimed mainly at the prevention of gas gangrene, but this complication is extremely rarely, if ever, seen in the face. On the other hand to do a cutting debridement of the face might needlessly sacrifice a feature—such as an eyelid, whereas these tissues have great recovery power, and to pack open a displaced nose or eyelid is to lose the best chance of repair—which is early.

It has been firmly established that if badly lacerated faces can be restored promptly—that the one single operative procedure can often effect an excellent result. The patient in Figure 1 represents this type of soft tissue injury, with almost no structure left undamaged in the area. By early evacuation and prompt surgical repair—without cutting debridement, or packing the wound open—this patient has had her complete result obtained in the one single operation. Without this early operation as satisfactory result would never have been attained, even with the twenty or thirty operative procedures that would have been necessary.

Pressure dressings on the face—especially, in fresh injuries, are as important as any place in the body. The use of fine, white cotton mechanics waste—now supplied as surgical waste—supplies an excellent medium of pressure—the final pressure of course being obtained with appropriate rolls of bandage. It is interesting that the first use of a pressure dressing recorded is in the

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Presented at the Meeting of the American Surgical Association, Hot Springs, Va., March 26, 1947.

\* Read before the American Surgical Association, March 26, 1947, Hot Springs, Va.

hieroglyphics and is in relation to facial wounds Edwin Smith Surgical Papyrus

The normal face, among other things needs protection of the eyeballs, a nose to breathe through and a mouth to allow normal eating These elements should guide the approach to the problem of repair of the badly injured face



FIG 1—Early evacuation and immediate operation One single operation for complete repair



FIG 2—Use of local tissue in one operation for repair Saliva turned back down the throat instead of out on chest

and in the mess of the acute injury such basic philosophy of treatment should not be lost sight of in the face of all the technical details This statement perhaps may appear trite, but to wind up a severe facial injury repair and fail to obtain an airway for instance, means needless discomfort and possibly permanent loss of normal function



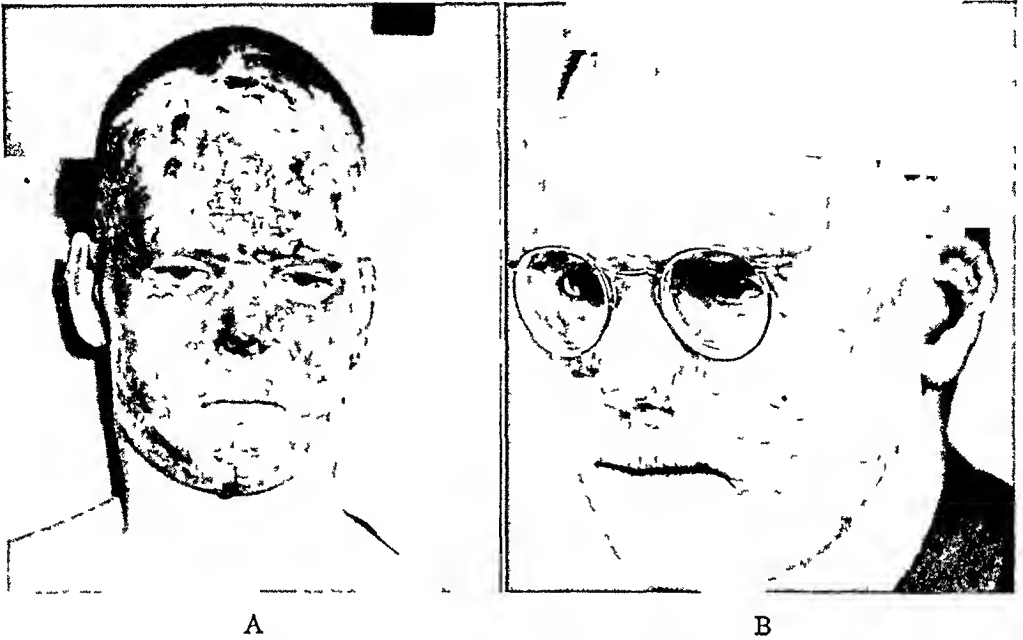


FIG 3—Total burn of face, grafted early to obtain healing. Contracted scars and imbedded whiskers dissected out later and full restoration done with free split skin grafts. Forehead, cheeks, lips, chin, eyelids and nose all grafted.

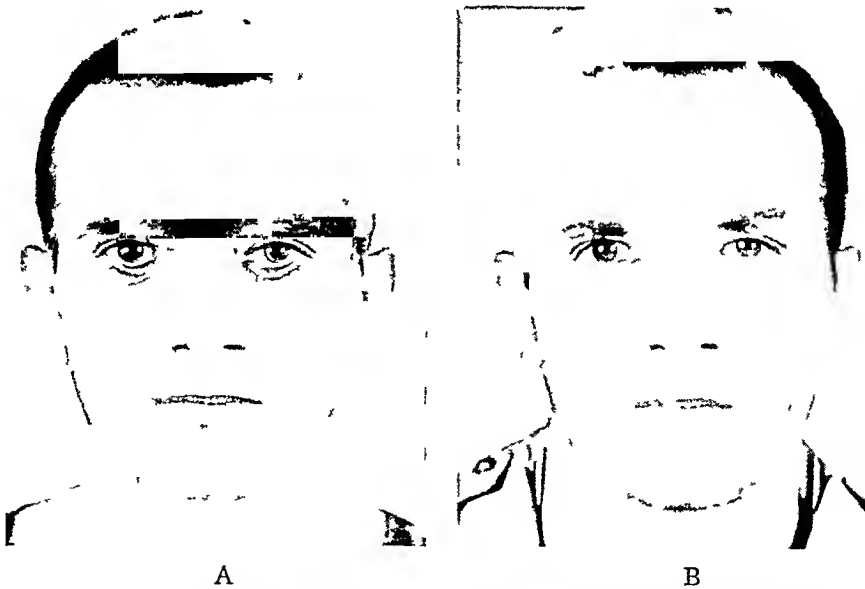


FIG 4—Free full-thickness grafts from clavicular region to recover lids after dissection of scar. Two lids done at one operation, no secondary trimming necessary.



Fig 5—Complete loss of chin and surrounding soft tissue, jaw gone from ramus to ramus, tongue fixed out on neck. Restoration with large lined flat flap from chest. Free graft to mobilize tongue, flap defect grafted at time it was used. Single bone graft of entire jaw from stump of ramus on one side to the other, done with single rib

In carrying out secondary repairs the following considerations and procedures are summarized

Local tissue is utilized when ever possible to effect repairs In Figure 2 this is well illustrated with the entire repair being done in one operation and the saliva turned back down the throat rather than out on the neck This fundamental which includes the use of the Z-flap is almost so obviously to be considered that it is some times not mentioned adequately All possible local tissue is always used whether additions are made or not (Figs 5 and 7) On



FIG 6—Practically total loss of covering of face from freezing (Early photo courtesy Dr E M Bricker) (Early grafting done by Doctor Hickey) Restoration in 18 operations Almost entire resurfacing of flat surfaces of face with free thick split grafts including orbital region Whole nose made from flat arm flap and preserved cartilage Ears made from scalp flaps, cartilage and split skin grafts (The loyalty of this patient's wife saved him for a normal life and they together are making their way)

the other hand the method should not be used when it will distort other features or interrupt important nerve supply One could hardly expect widespread losses from burns about the eyelids and cheeks and nose to be subject for this treatment, and there frequently must be new tissue added

The ability to add new tissue is the "sine qua non" of the plastic surgeon and the following necessary instances of supplying new tissue are presented

Burns require free skin grafts most extensively—free grafts are preferable on flat surfaces to thick flaps because of finally being more expressive, there being little emotional expression possible through or under a thick flap Fig-

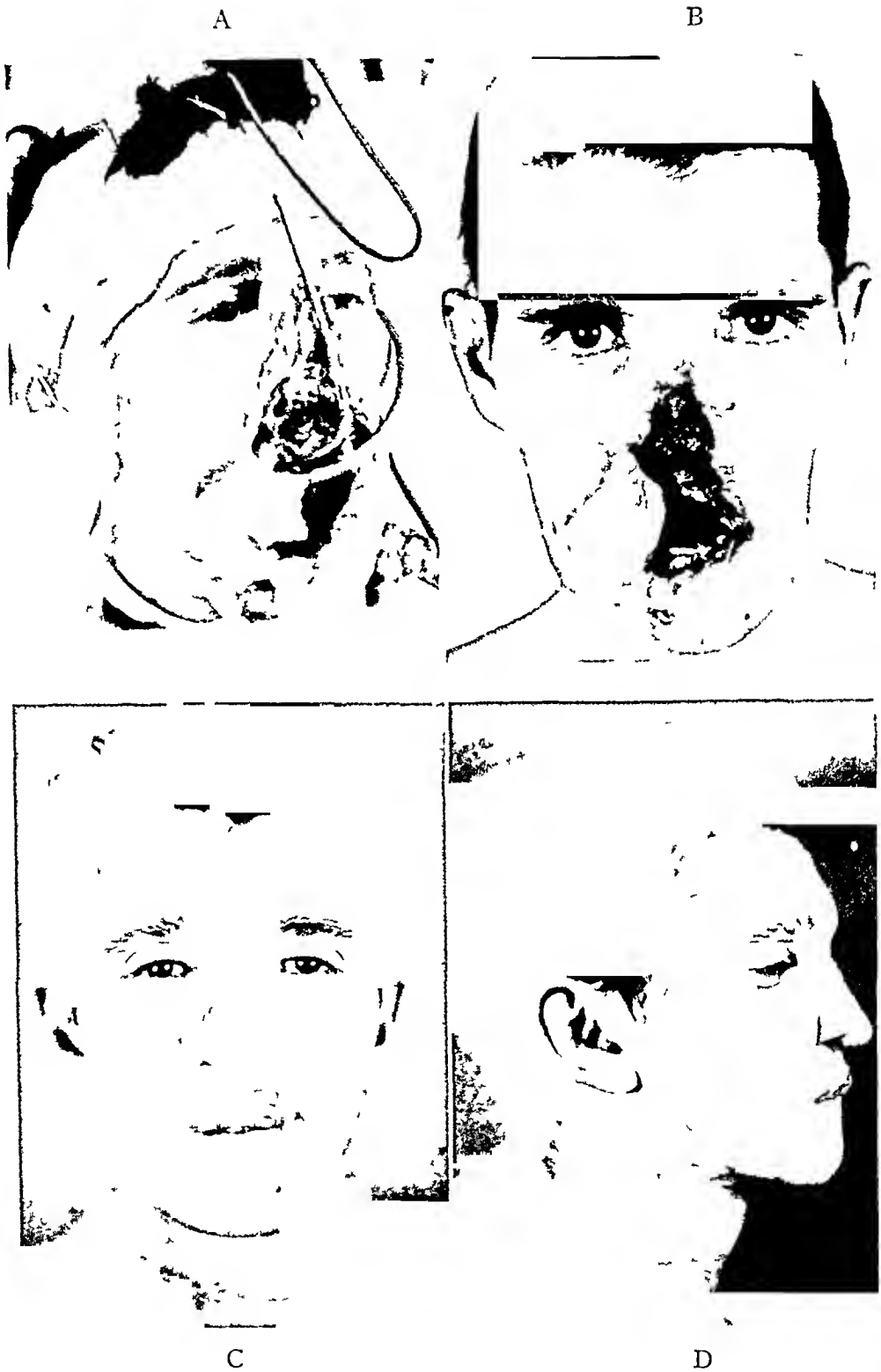


FIG 7—One of the worst types of composite and compound injury. Restoration with local tissue, free skin grafts and flat flap from arm for nose. Cancellous bone graft for jaw. Cartilage support for nose.

ure 3 represents almost a complete replacement of the skin of the face with free skin grafts, both cheeks, forehead, lips, chin, eyelids, and nose being covered. The skin of the anterior chest wall just below the breast is usually best for the flat areas of the face.

Free full thickness grafts from the clavicular region, have been recently utilized to excellent advantage on the eyelids and nose. The color best matches the face and the function is excellent. The patient in Figure 4 illustrates the total resurfacing of the lids with these grafts without the necessity of any secondary trimming of the edges.



FIG 8—Use of distant flap for nose, rather than cut into forehead. Flat flap from arm used. Cartilage for support and final color obtained with permanent pigment injection. Patient has only travel vision.

Total losses of areas as in Figure 5 require flap restoration of the soft parts and finally support for the soft tissue restoration. (The plastic surgeon has to build somewhat backward, putting in the outside or covering first and the support later.) This patient has had a free graft under the tongue to allow movement. Then a lined flat flap from the chest made the chin, lip and floor of mouth. This closed the mouth, turned the saliva back down the throat and permitted his taking food. The flap is a flat one, turned in for lining, not tubed. The defect of its bed is grafted at the time it is used.

Restoration of the jaw has been done as in Figure 5, putting in the entire body with a rib transplant—extending from ramus to ramus. It is planted in the new flap first and then attached to the remnants of the ramus later. The restoration of this patient is far short of his worth and the surgeon's wishes for him but it is adequate for him to follow a normal life.

## FACIAL INJURIES

Cancellous bone from the ilium is used extensively in jaw replacements and probably gives the best overall chance of healing (Fig 7)

*Freezes of the face* are apt to be widely destructive as in Figure 6 This patient has had almost his whole face resurfaced with free grafts including the whole region of the orbit The nose and both ears have been totally reconstructed

*Noses* are usually made from forehead or neck flaps, but as in the above patient (Fig 6) it has been made from an arm flap In Figure 7 the nose has also been made from an arm flap as shown—in this patient the forehead was too narrow In Figure 8 the arm has been used to avoid scarring the forehead The final color match was obtained in this patient by pigment injection

*Ears* are usually made from a local scalp flap, a cartilage transplant and a free skin graft Both ears on the patient in Figure 6 were made at the same



FIG 9—Composite free graft of two surfaces of skin and intervening cartilages from ear for nasal reconstruction One single operation Repair of ear with scalp flap

time in three operations (as reported in S G & O, February, 1947) If desirable a short tubed neck flap can be added

*Composite grafts of skin* and cartilage from the ears have been used extensively for repairs of the nose as shown in Figure 9 and as reported previously in the ANNALS OF SURGERY October 1946 and Surg Gyn and Ob April 1946

*Cartilage* is usually used to support noses as in Figures 6 and 7 The transplant is cut in an L-shape in one piece and may be homogenous, autogenous or preserved Cartilage is also used in chips and grated to fill defects that can be molded into shape and don't require too much support Cartilage for ears is essential and if the angle of a costal cartilage is available a good shape of an ear may be cut out of it

As can be noted there is a composite picture of care in the restoration of these patients, the original life saving work just after the accident, the endless

nursing care, and the cooperation and work of the ophthalmologist, the rhinologist and the dental surgeon. The endless detail and dressing care and operative work that is supplied by house surgeons and younger surgeons is recognized as essential for the recovery of these patients.

These patients are still individuals and have all the problems of getting along that anyone does, and they should not be grouped as a class, or given up because of their difficulties. The work often appears endless both for the patient and the surgeon—and the surgeon too well realizes that the best result will be short of his wishes or of what the patient deserves. But slow progress can be made, of lessening the time required in the repair, of improved technical work, and of making good work more easily available through observation, recording and teaching.

**DISCUSSION**—**DR LEO ELOESSER**, San Francisco. In expressing the universal recognition of these truly dramatic results, I would like to add one word, to say that the prepuce, if available, may be used for making pretty good eyelids. If one circumcises the patient and splits the prepuce part way so as to shape it into the form of a pair of trousers, one leg of this free graft will make an upper lid and the other a lower lid.

**MR H ECKHOFF**, London, England. It is very difficult to know what to say about the paper of Dr Barrett Brown. We were lucky enough to have Doctor Brown with us once or twice. In the main we carried out these special restorations in the same manner that Doctor Brown has shown you, the only marked difference being in rhinoplasty. The use of the flap from the ear is more common in the States than in England. At East Brimsted, where I did most of my work we used the forehead almost entirely for these reconstructions. There were of course many cases where that was not possible, cases in which the forehead had been extensively damaged from bombs or by other injuries. In those instances we preferred to use the thoracic pedicle, with the thought that the arm-to-nose position was uncomfortable for the patient. Even when we have completed as much as we can, these people do lack a good deal of what we would like for them. Nevertheless, as you see them in the mass, see them individually and get to know them, you realize how wonderful it is to be able to help them, even to a limited extent.

**DR JAMES BARRITT BROWN**, St Louis (closing). I want to thank Doctors Eloesser and Eckhoff. In replying to Doctor Eloesser's suggestion, the only prepuce grafts we saw on eyelids became so black that we had to remove them and replace them with other grafts. If they would stay light, they would probably be satisfactory.

### EDITORIAL ADDRESS

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## SUBTOTAL GASTRECTOMY FOR GASTRIC ULCER A STUDY OF END RESULTS\*

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GASTRIC ULCER differs in a number of respects from duodenal ulcer, a lesion with which it is often discussed and even confused under the common term peptic ulcer. Gastric ulcer is characterized by certain features which are lacking in duodenal ulcer and which exert an important influence upon the management of the disease. These several peculiarities may be summarized briefly as follows: (1) the existence of ulcer, its exact location, size and other characteristics can be demonstrated by roentgenologic examinations and/or gastroscopy in a high percentage of cases, (2) the response to treatment may be very accurately followed and recorded by these same methods, (3) it is often closely mimicked by primary ulcerating carcinoma, (4) carcinomatous degeneration may occur as a late complication of an originally benign chronic gastric ulcer, (5) surgical intervention is required in a larger percentage of cases than in the case of duodenal ulcer, (6) practically all surgical procedures, including the simpler ones, will substantially reduce the gastric acidity, (7) the clinical results of operative treatment are better than in duodenal ulcer and (8) anastomotic ulcer is a rare complication following gastroenteric anastomoses for gastric ulcer.

While during recent years the mortality of all gastric operations and particularly that of resection has steadily declined until it has reached a reasonably satisfactory level, the differentiation of benign ulcers, malignant ulcers and ulcerating carcinomas, remains a vexing clinical problem and one which is far from a satisfactory solution at the present<sup>1, 2</sup> time. These difficulties in accurate differential diagnosis have prompted certain authors, notably Allen and Lahey<sup>3</sup> to take the position that gastric ulcer, unlike duodenal ulcer, is primarily a surgical problem and that, except in certain unusual circumstances, surgical treatment should be advised once the diagnosis is made. They believe that by such a plan fewer lives will be lost from operative deaths than will be the case when gastric cancers are treated medically under a mistaken diagnosis. Other writers, outstanding among whom is Heuer<sup>4, 5</sup> question the propriety of

\* Read before the Meeting of the American Surgical Association, March 25-27, 1947, Hot Springs, Virginia



such a radical attitude and especially with regard to gastric resection. The objections usually raised are (1) an operative mortality that is still appreciable, (2) the unsatisfactory clinical results with or without recurrent ulceration which are seen in the occasional patient, and (3) the late nutritional disturbances which are observed in some cases after subtotal gastrectomy.

In order to formulate a working policy in regard to this matter for our own use in the future, we have endeavored to answer some of these questions on the basis of our own past experience. The present studies, therefore, represent an attempt to (1) ascertain the risk involved in operation and to some degree the incidence of malignant growth, (2) make a critical analysis of clinical end results as far as the ulcer problem is concerned, and (3) discover the incidence and severity of certain side-effects of the operation, such as post-resection symptoms, nutritional disturbances, blood disorders, etc.

#### CLINICAL MATERIAL

During the 20 years that have passed since the University Hospital received its first patient in late 1925, 1356 patients with gastric ulcer have been observed and treated on the medical and surgical services. Of this number, 246 patients or 18.9 per cent required surgical intervention. The incidence of surgical treatment during the last 3 years of this study (1943, 1944 and 1945) was just over 30 per cent. Twenty of these 246 patients exhibited acute perforations of a gastric ulcer and required emergency surgical therapy. Since, in such cases, the problem is unique and about it there is no difference of opinion, these 20 cases will not be considered further. Elective surgical procedures were performed in 226 cases. The yearly incidence of all gastric ulcers, as well as of those treated surgically by year, is outlined in Figure 1. This graph also illustrates an experience which has been common in all surgical clinics, *ie*, the decline in popularity of the more conservative operations such as gastroenterostomy and knife or cautery excision of the ulcer either singly or in combination, in favor of the more radical procedure of gastric resection. The latter procedure has, here as elsewhere, become the operation of choice in the treatment of gastric ulcer during these past 20 years when 188 partial, subtotal or total gastrectomies have been performed. Whether this procedure, while admittedly giving satisfactory results as far as cure of the ulcer is concerned, will remain the best one for the lesion under discussion, may be questioned by some in view of the dramatic results now being reported from vagal interruption for both gastric and duodenal ulceration. Certainly it is true that additional experience with this newer procedure will be required and a longer time interval for further observations will be necessary before a final evaluation can be made. In view of the ever-present danger of potential or existent carcinoma in ulcers proximal to the pyloric valve, it seems likely that subtotal gastrectomy will continue to hold an important position in the surgical field for the treatment of lesions in this location. In the meantime, it is well from time to time to assess the value of and consider the true worth of this operation in view of the evidence which has now accumulated. For that reason an intensive follow-up

GASTRIC ULCER

survey of cases treated by gastrectomy during the past 20 years has been undertaken in order to consider the late end results. Some patients have been followed for as long as 20 years and a considerable number have been followed from the time of operation to their death from whatever cause many years later. Thus an overall survey is possible and certain more or less final conclusions can be drawn.

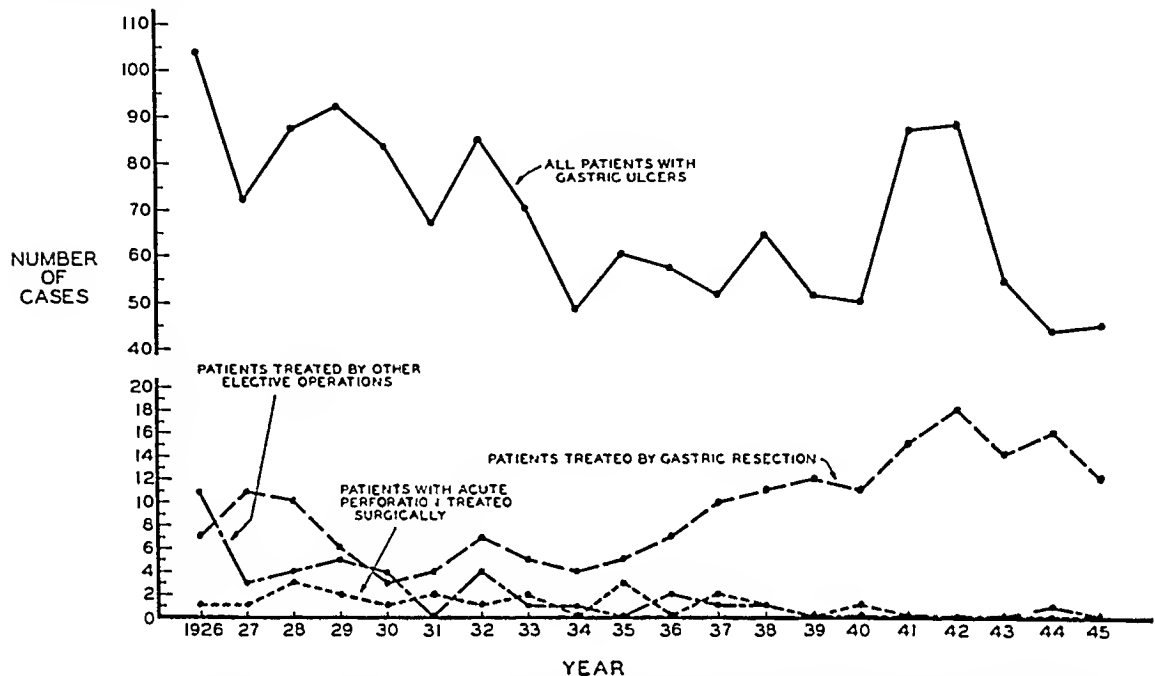


FIG 1—Graph showing yearly incidence of all gastric ulcers and those treated surgically. Surgical treatment was carried out in 18.9 per cent of the entire group (including acute perforations) and in 30.5 per cent (all elective operations) during the last three years.

DISTRIBUTION OF MALIGNANT GASTRIC ULCERS  
(19 CASES)

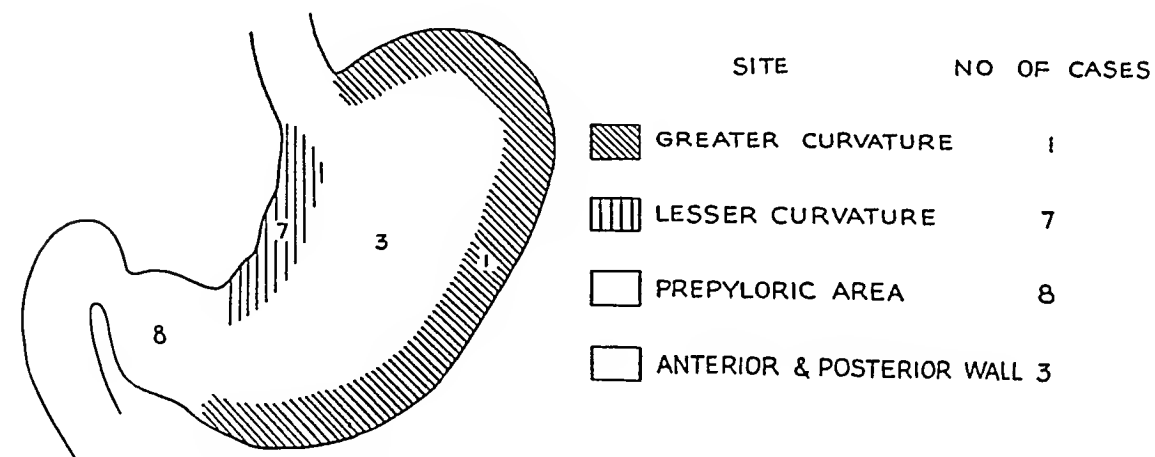


FIG 2—Diagram showing location of 19 "malignant ulcers"

The group of 188 patients under consideration consisted of 154 men and 34 women whose ages range from 29 to 74 years, the average age being 52.3 years. In all cases, with the exception of one, in which a palliative gastrectomy<sup>6, 7</sup> was performed, the ulcer was removed at operation and subsequently

investigated by histologic study. While in many cases the preoperative diagnosis was that of possible malignancy, in all cases at operation it was the opinion of the operator that he was dealing with a benign lesion, as no unusual features which led him to suspect malignancy were noted in either the lesion itself or the regional lymph nodes. Accordingly the usual type of ulcer resection was carried out without resorting to wide removal of omenta or lymph node bearing areas. Moreover gross examination of the surgical specimen in no case revealed conclusive evidence of malignancy. In the last analysis, however, as the result of microscopical studies, 19 patients or 10.1 per cent were found to have malignant disease superimposed upon an old chronic ulcer. The

### DISTRIBUTION OF BENIGN GASTRIC ULCERS (169 CASES)

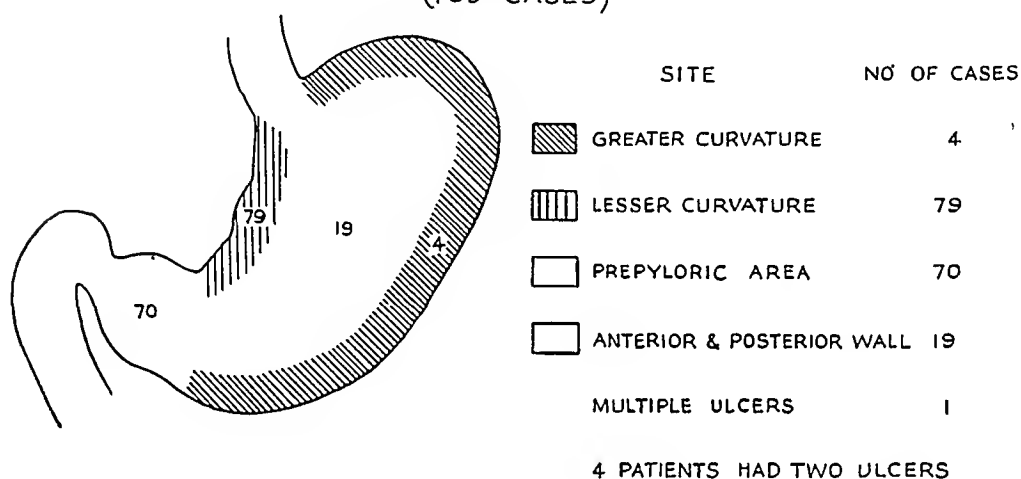


FIG 3—Diagram showing location of 169 benign gastric ulcers

location of these malignant ulcers is shown in Figure 1. In all of the remaining 168 cases, the diagnosis of a benign ulcer was confirmed by the pathologist. The location of the benign ulcers is shown in Figure 2. Four patients had two independent and coexistent gastric ulcers, while in one case there were multiple ulcers of the stomach and duodenum. In 31 of the 188 cases an associated duodenal ulcer, either active or healed, was also present as noted at the time of operation. In every case, however, this lesion was of secondary importance and the behavior of the gastric ulcer governed the treatment of the patient.

#### INDICATIONS FOR OPERATION

During the 20-year period under discussion a conservative attitude in treatment has been shared by members of both the medical and surgical departments as far as peptic ulcer is concerned and relatively few patients have been advised to have surgical therapy unless there was convincing proof as the result of a fair trial of thorough medical treatment that no other measures would suffice. In Table I the original indications for surgical intervention in these

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TABLE I  
GASTRIC RESECTION FOR GASTRIC ULCER  
INDICATIONS FOR SURGERY

Chief Indication	No of Cases	Per Cent
Intractable to Conservative Treatment	69	36.7
Probable Carcinoma	56	29.8
Obstruction	41	21.8
Penetrating ulcer	10	5.3
Hemorrhage	9	4.8
? Perforation	3	1.6
Total	188	100.0

188 cases are summarized. Although frequently there were several factors which combined to indicate surgery, for the sake of simplicity the most important one has been selected for this tabulation. While in practically all cases the possibility of malignancy was present in 56 cases or 29.8 per cent a clinical diagnosis of probable carcinoma was made on the basis of all of the data available. This diagnosis was entertained in view of the age of the patient, the short clinical history, achlorhydria, roentgen studies and gastroscopy, considered either singly or in combination. In five instances large ulcers on the greater curvature of the stomach strongly suggested a malignant lesion and in others the prepyloric location increased the likelihood of malignancy since Holmes and Hampton<sup>8</sup> have found 65 per cent of prepyloric ulcerating lesions to be malignant. The largest group, *i e*, 69 patients or 36.7 per cent, were proven beyond peradventure of a doubt to have lesions quite intractable to conservative measures. These ulcers failed to heal or to remain healed or as not infrequently happened actually increased in size while a strict medical regimen was in progress. They were, therefore, necessarily regarded as malignant ulcerations or calloused benign ulcers which could not be closed by conservative measures and accordingly surgery was in order. Persistent obstruction failing to yield to conservative means was largely responsible for the necessity of surgical intervention in 41 patients or 21.8 per cent of the group. Repeated bouts of alarming hemorrhage required surgical therapy in 9 cases or 4.8 per cent and in a considerable number of other patients bleeding was an important item in the clinical history. There were no instances in this series of emergency surgery for acute massive hemorrhage. In three cases operation was performed during an episode of acute abdominal symptoms which strongly suggested an acute perforation. An incorrect diagnosis was proven at laparotomy, at which time, however, resection was performed. In ten cases the fact that roentgenograms showed evidence of a deeply penetrating ulcer constituted the indication for surgery. In summary, it may be said that in almost every case in which operation was performed malignancy could not be positively excluded and, if for no other reason, the operation was justified on the assumption that that particular lesion was a possible or probable carcinoma.

A summary of the status of the medical program, prior to operation, is given in Table II. It will be observed that exactly one-half of these cases

TABLE II  
GASTRIC RESECTION FOR GASTRIC ULCER  
STATUS OF MEDICAL TREATMENT

Character of Treatment	No of Cases	Per Cent
Adequate or intensive In hospital	95	50.5
None	53	28.2
Brief	29	15.4
None Much elsewhere	11	5.9
Total	188	100.0

received an intensive course of medical management in the hospital before being advised to accept surgical treatment. In all of these cases the evidence was convincing that further attempts at conservative therapy would be useless. Eleven patients or 5.9 per cent were referred by their home physicians for surgery. They had all received good medical management by their physicians before coming to the hospital and for them any further attempt at medical treatment was thought superfluous. Because of the strong presumptive evidence of malignant disease, surgical treatment was carried out at once in 53 cases or 28.2 per cent. Twenty-nine patients or 15.4 per cent were given a trial of conservative treatment but when because of persistent obstruction, continued bleeding or constant pain it became apparent such treatment would not succeed, surgery was undertaken at an early date.

#### TYPE OF OPERATION

In Table III the several types of operation which were performed in the 188 cases are listed. During the past decade our preference has been for the

TABLE III  
TYPE OF OPERATION—188 CASES

Operation	No of Cases	
Polya		
Antecolic	3	
Retrocolic	44	47
Hoffmeister		
Antecolic	15	
Retrocolic	113	128
Finsterer		6
Finsterer (?)		2
Finsterer-Bancroft		1
Palliative gastrectomy		1
Total gastrectomy		3

Hoffmeister type of reconstruction with a retrocolic anastomosis if and when technically feasible. Partial closure of the cut end of the gastric pouch has seemed to reduce the incidence of malfunctioning stomas during the early post-operative period and to avoid too rapid emptying of the stomach later. The removal of practically all of the lesser curvature, a desideratum in the treatment of peptic ulcer, especially when duodenal ulcer is present, is likewise facilitated. In the first decade from 1926 to 1936 the posterior Polya reconstruction was the procedure most often employed.

Total gastrectomy was performed in three cases in all of which the ulcer was situated high on the lesser curvature or on the posterior wall and had proven quite intractable under most intensive medical treatment. The radical complete gastrectomy was elected at the time of laparotomy in the belief that the lesion must be malignant, whereas subsequent microscopic studies in all three cases revealed it to be benign. With the mortality of total gastrectomy still relatively high and with the higher incidence of post-resection symptoms, it is questionable whether total gastrectomy should often be performed for benign ulcer. In the future, for such lesions, we would suggest excision of the ulcer in order to have tissue for microscopical examination, in combination with vagotomy and with or without a complementary gastric drainage operation. A second alternative is the transthoracic resection of the upper portion of the stomach as suggested by Sweet.<sup>9</sup>

Palliative gastrectomy as recommended by Colp was performed in only one case. This patient had a large gastric ulcer high on the lesser curvature and also an old duodenal ulcer which made the dissection of the upper portion of the duodenum a tedious and time-consuming task. In order to avoid the risk of an exceptionally high sub-total or even total resection, the ulcer containing segment of the duodenum and the lower two-thirds of the stomach were resected leaving the gastric ulcer *in situ*.

Finsterer's<sup>10</sup> resection for exclusion as usually performed for very active duodenal ulcers has been followed by a high incidence of stomal ulcer in the experience of practically all surgeons and has now generally been discarded. Six such Finsterer procedures were noted in this series. All of these operations were performed in the early years when the importance of elimination of all of the antral mucous membrane was not fully appreciated. In all cases the gastric ulcer was removed, but this procedure was elected when inflammation about the pylorus would have made a dissection beyond it dangerous and the closure of the duodenal stump difficult and uncertain. It would seem from a perusal of the operative notes in two additional cases that the lower transection was just proximal to the pylorus and that the operation which was performed was probably a form of the Finsterer exclusion operation. Presumably this prepyloric transection was used in order to expedite the operation in that particular case. In one instance in which the Finsterer type of resection was intentionally performed, the mucosa of the antral segment was carefully dissected out and removed as suggested by Bancroft.<sup>11</sup>

#### OPERATIVE MORTALITY AND POSTOPERATIVE COMPLICATIONS

There were 15 operative deaths in the aforementioned 188 resections—a mortality of 7.9 per cent. The causes of death are listed in Table IV. In gastrectomy as in all other operations of similar magnitude, the mortality has decreased steadily during recent years. Better preoperative and postoperative care as well as the better methods of anesthesia now available, have been responsible for increased experience with the operation and standardization of the technic. It will be noted that pneumonia was the largest single contributor

TABLE IV

GASTRIC RESECTION FOR GASTRIC ULCER—188 CASES  
Operative Deaths—15      Mortality—7.9 Per Cent

Cause of Death	Cases With Autopsy—8	Cases Without Autopsy—7
Pneumonia	3	1
General peritonitis—leak at gastro enteric anastomosis	3	
Pancreatic fat necrosis	1	
Volvulus of afferent limb of jejunum		
Peritonitis	1	
Wound disruption		1
Uremia		2
Shock		2
Acute vascular accident (pulmonary embolism or coronary thrombosis)		1

to the operative mortality, as four patients or over one-quarter of the group died from that complication. With the advent of chemotherapy and the antibiotic agents, this menace to success has been substantially reduced. The three deaths due to general peritonitis, all of which were the result of a leaking suture line, of course represent surgical errors, whereas the case of pancreatic fat necrosis and the one of volvulus of the jejunum are examples of surgical accidents possibly unavoidable but nevertheless regrettable. The volvulus of the jejunum occurred in a total gastrectomy in the proximal limb used for the anastomosis in a reconstruction after the method of Roscoe Graham<sup>12</sup>. Two cases are listed as dying of uremia. Since autopsies were not performed it is possible that peritonitis was primary with secondary renal suppression. In one of these cases a nephrectomy had been performed previously and here renal insufficiency is more probable. Likewise, in the two patients recorded as dying of surgical shock, autopsies were not permitted. Both patients died a few hours after return from the operating room and, since there was nothing unusual about their particular lesions and no complications had arisen during the operative procedure, they perhaps may be best classified as anesthetic deaths.

In making a final appraisal of the end results of gastric resection in the treatment of ulcer, not only must the clinical results over a number of years be considered but also the primary operative mortality. Our overall mortality rate of 7.9 per cent seems high at the present time and as such would serve as an indictment against the procedure. However, it must be borne in mind that most of these deaths occurred prior to 1936 and that the mortality has been greatly reduced in recent years. Many personal series composed of private patients would show a considerably lower death rate.

Table V gives the non-fatal postoperative complications, 64 such complications having been observed among 53 patients. It will be noted that major or minor wound sepsis constituted the largest group. These wound infections ranged from stitch abscesses to three cases of disruption in which a secondary operation for closure was required. It will be noted by referring to Table IV that in one case wound disruption was responsible for a fatal outcome, thus forcibly emphasizing the fact that disruption remains a serious complication.

## GASTRIC ULCER

and carries a high death rate. Pulmonary complications occurred with disturbing frequency as there were 13 cases of bronchopneumonia, 8 of atelectasis and 1 of lung abscess. The latter lesion was post-pneumonic in origin. In recent years pulmonary complications have been reduced in frequency and severity by virtue of chemotherapy, early ambulation, better management of abdominal distention, improved anesthesia, tracheo-bronchial suction and aspiration bronchoscopy. In the two cases of postoperative intestinal fistula, fortunately, both closed spontaneously. They indicated either leakage at the anastomosis or more probably a small blow-out of the duodenal stump. The single example of a subdiaphragmatic abscess probably occurred by the same mechanism. The case of sulfonamide hepatitis occurred at a time when large quantities of sulfanilamide powder or crystals were introduced into the peritoneal cavity at the time of laparotomy as a prophylactic measure. In this case

TABLE V  
GASTRIC RESECTION FOR GASTRIC ULCER  
NON-FATAL POST OPERATIVE COMPLICATIONS  
(64 complications among 53 patients)

Complication	No. of Cases
Wound sepsis	17
Broncho-pneumonia	13
Urinary tract infection	10
Pulmonary atelectasis	8
Wound dehiscence	3
Ileus	3
Intestinal fistula	2
Auricular fibrillation	2
Subphrenic abscess	1
Lung abscess	1
Cerebral hemorrhage	1
Thrombophlebitis	1
Abortion	1
Sulfonamide hepatitis	1

there was intense jaundice but spontaneous recovery took place without sequelae. The other complications for the most part occurred singly and were not serious. Urinary tract infections were fairly frequent but fortunately all terminated promptly under appropriate therapy.

## MALIGNANT ULCERS

In 19 cases or 10.1 per cent the microscopical examination of the operative specimen disclosed unmistakable evidence of malignant disease. In none of these cases was suspicion sufficiently aroused at the time of operation to alter the course of the operative procedure and the usual ulcer resection was performed. The operative notes in these cases indicate findings identical with those of the lesions microscopically benign, and in none of these cases were the regional lymphnodes found noteworthy and accordingly extensive resection of lymphnode-bearing areas or omentectomy were not performed. In 17 of the 19 cases microscopical study revealed an early or even advanced carcinoma developing on the basis of an old chronic peptic ulcer. In all of these cases the original lesion was definitely an ulcer with the carcinoma



superimposed and none were primary ulcerating carcinomas. Two cases showed at the edge of a chronic ulcer an area of lymphosarcoma. In this group of 19 patients with associated malignant disease, there were 15 men and 4 women. The two lymphosarcoma cases occurred in male patients. The age range for this group was 30 to 67 years, with an average of 56 years. This average age is slightly higher than that for the entire group which was 52.3 years or for the group of 169 benign lesions where it was 52.2 years. In 12 of the ulcer-cancer cases special studies of the regional lymphnodes attached to the operative specimen were made. In four there was involvement by metastatic carcinoma while in eight the nodes were negative. The regional lymphnodes in one of the lymphosarcoma cases revealed evidence of neoplasm. In view of the ultimate diagnosis of malignancy in this group, it is interesting to reconsider the status of the preliminary medical program. Three patients had had prolonged and intensive medical treatment elsewhere before entering the hospital and surgery was advised at once. In 9 cases there was no delay and for one reason or another prompt surgical intervention was recommended, whereas in 7 cases considerable valuable time was spent in unsuccessful medical treatment by us, and surgery was performed only when check-up roentgenograms showed failure of the ulcer to improve. There was one operative death in this group which has already been referred to as an anesthetic death.

The follow-up studies in this group are of special interest (Table VI). In addition to the patient who died in the hospital, another patient, a woman, returned as an emergency exactly one month after her discharge and required a tracheotomy for upper respiratory tract obstruction due to necrosis of the cricoid cartilage. This lesion was undoubtedly due to the prolonged use of a Levine tube for Wangensteen suction during the postoperative period. She died shortly after her return from the operating room. In addition to these two cases, six other patients have since died. All six with one exception have died of recurrent carcinoma. This latter patient survived for seven years and eight months free from recurrence and in good health and died of a cerebral hemorrhage. The survival period of the patients who died of malignant disease (excluding the one operative and the one early postoperative death) ranged from seven months to three years and seven months, the average being 24.6 months. Eleven patients of this malignant group are still living, their survival periods ranging from one year to seven years and ten months. All of them are in good health at the time of this report with one exception. This patient reports that his health is poor but in view of the fact that he has survived for six years and six months recurrence seems improbable. The two lymphosarcoma patients are both living and in good health at the present time.

In summarizing this group of 19 patients with microscopically verified malignancy associated with a chronic gastric ulcer, 7 or 36.9 per cent have now survived for more than five years, but if the two postoperative deaths are excluded, the five-year survival rate becomes 41.2 per cent. This is similar to the findings of Allen, who reported a 40 per cent five-year survival rate

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TABLE VI

GASTRIC RESECTION FOR GASTRIC ULCER  
GASTRIC ULCERS—MALIGNANT  
END RESULTS IN 18 PATIENTS WHO SURVIVED OPERATION

Survival Period	Living	Dead
Less than 1 year		2
Over 1 year	1	2
Over 2 years	1	1
Over 3 years		1
Over 4 years	3	
Over 5 years	2	
Over 6 years	1	
Over 7 years	3	1
7 Five year survivals =		
36 8 per cent including operative deaths		
41 2 per cent excluding operative deaths		

TABLE VII

GASTRIC RESECTION FOR GASTRIC ULCER—1926-1945 INCLUSIVE

1 Cases included in present study of end results	138
2 Cases which have been followed for less than two years	17
3 Cases of gastric ulcer with superimposed malignancy—microscopical evidence	19 (10 1%)
4 Operative deaths	15 (7 9%)
5 Total number of resections performed	188
(One case is included in both groups 3 and 4)	

including operative deaths in a similar group of malignant lesions. When it is remembered that the number of five-year survivals in the average reports of cancer of the stomach is in the neighborhood of 20 per cent of the cases resected, it becomes apparent that an aggressive attitude toward gastric ulcer should assist in improving the present poor results in the treatment of gastric carcinoma.

METHOD OF EVALUATION OF END RESULTS

It is a well-known fact that a final judgment of the results of treatment is possible only after many years when one is studying a lesion such as gastric or duodenal ulcer. For that reason we have arbitrarily excluded from final consideration all patients who have not been observed for at least two years postoperatively. This automatically eliminates 12 patients who were operated upon during 1945 as well as five others operated upon earlier but who died of intercurrent disease in less than two years. There have been no unsatisfactory results in these groups.

There remain 138 cases (Table VII) suitable for evaluation of end results and these have been followed for periods ranging from two to 20 years. Data are available on all of these patients. The information has been obtained principally through return visits for check-up examinations, but also by letters, questionnaires and telephone conversations with both patients and their physicians and finally, in case of death, from the Michigan State Department of Health. The follow-up study has been a continuous one, having been inaugurated many years ago. For the present purpose, the various reports for each patient have been assembled and a rating given based upon the combined

evidence Emphasis has been placed upon the most recent reports inasmuch as occasionally a shift in position up or down the scale becomes necessary, even after a number of years As a rule changes have been for the better,

TABLE VIII

## DURATION OF FOLLOW-UP STUDY—155 CASES

Number of Years After Operation	Living	Dead
Less than 2 years	12	5
2-5	43	14
5-10	34	10
10-15	10	10
15-20	9	7
Over 20		1
Total	108	47

TABLE IX

## GASTRIC RESECTION FOR GASTRIC ULCER

## CAUSE OF DEATH IN 47 PATIENTS WHO HAVE DIED SINCE DISCHARGE

Cause of Death	No of Cases
1 Cardio vascular disease	18
Cerebral hemorrhage	7
Cardiac disorders (including coronary thrombosis)	9
Rupture aneurysm aorta	1
General arteriosclerosis	1
2 Pulmonary disease	9
Pneumonia	5
Pulmonary tuberculosis	3
Lung abscess	1
3 Trauma	8
4 Jejunal ulcer	3
5 Renal disease	2
Pyelonephritis	1
Chronic nephritis	1
6 Miscellaneous	7
Carcinoma of remaining gastric pouch	2
Carcinoma of colon	1
Meningitis	1
Alcoholism	1
Suicide	1
Unknown	1

TABLE X

## SUMMARY OF END RESULTS OF GASTRIC RESECTION FOR BENIGN GASTRIC ULCER

Type of Result	No of Cases	Per Cent
1 Excellent	86	62
(a) Completely symptom free	65	
(b) Very slight symptoms	21	
2 Good	41	30
3 Poor	7	5
4 Jejunal ulcer (verified)	4	3
Total	138	100

Satisfactory results in 127 cases = 92 per cent

although occasionally the reverse is true For example, some patients who for a time were classified as only improved, because of their inability to regain strength or maintain proper weight have finally overcome this trouble and have been shifted to the excellent group Again certain other patients whose

residual symptoms were principally related to the small size of the remaining stomach have in time compensated for this difficulty and now remain among the excellent result cases. Patients who have developed jejunal ulcers and most of those who have obtained poor results have had a poor record from the beginning. For convenience a classification consisting of four categories has been employed. These are (1) Excellent, (2) Good, (3) Poor, and (4) Jejunal ulcer (verified).

In Table VIII the duration of the follow-up study is analyzed and here it will be seen that 108 patients are still living and 47 are dead. These figures include for completeness the 17 cases under two years which are not included in the final calculations. Table IX gives the causes of death in the 47 patients who have died. It will be observed that death in three cases was due to jejunal ulcer and, in fact, it occurred following secondary or tertiary operations for this condition.

### REMOTE RESULTS

In general the end results have been extremely satisfactory and in only 11 cases or 8 per cent have definitely unsatisfactory results occurred (Table X). One hundred twenty-seven patients or 92 per cent have entirely satisfactory results, whereas 86 of these can be classified as excellent.

1 *Excellent results* This is by far the largest group and is composed of 86 patients or 62 per cent. Sixty-five patients or 75 per cent of this group and 47 per cent of the entire series are completely symptom free and restored to a state of normal health. They eat normally without restrictions, are entirely rehabilitated as far as their economic or social status is concerned and suffer

TABLE XI

#### GASTRIC RESECTION FOR GASTRIC ULCER SUMMARY OF CASES WITH EXCELLENT RESULTS—86

Completely symptom free	65
Minimal symptoms	21
Slight weakness	6
Slight intolerance to certain foods	19
Fats	9
Condiments etc	6
Coarse foods	5
Acid foods	3
Sweets	2
Coffee	1
Ice cream	1
Milk	1
Soft drinks	1
Alcoholic liquors	1
Nuts	1

no postresection symptoms. Even on careful questioning no complaints can be elicited. The remaining 21 patients in this group of 86 are also considered as having excellent results. They are well, free from their ulcer symptoms, but on careful questioning report trivial, insignificant or inconsequential symptoms. The latter are not disturbing and consist either of slight weakness or slight intolerance to certain foods (Table XI). A group of normal individuals

would probably show a similar incidence of such symptoms. Fatty foods, for example, pork, fried foods, gravies and rich pastries are troublesome for the largest number of patients. Second in importance are the highly seasoned foods, *e g*, pickles, condiments, spices, etc., and third, coarse foods with considerable residue, such as radishes, cucumbers, celery, cabbage, etc. None of these patients requires a special diet and all can remain symptom free by merely avoiding the objectionable items. As far as these 86 patients are concerned the results may be cited as among the best seen following any type of surgical operation of similar magnitude.

TABLE XII  
GASTRIC RESECTION FOR GASTRIC ULCER  
Analysis of Good Results 41 Patients

Symptoms		No of Cases		
Weakness		11		
Symptom free but adhere to diet		3		
Referable to small size of stomach		11		
Referable to hypoglycemic or 'dumping' syndrome		9		
Specific food intolerance		18		
Fats	13	Sweets	4	
Coarse foods	6	Milk	3	
Condiments etc	6	Acid foods	1	
	*	*	*	*
Symptoms partially or wholly due to associated disease—20 patients				
Arthritis	4	Hemochromatosis	1	
Cholelithiasis	3	Macrocytic anemia	1	
Heart disease	3	C N S lues	1	
Carcinoma of gastric pouch	2	Ch nephritis	1	
Carcinoma of colon	1	Pul tuberculosis	1	
Diabetes	1	Hypertension	1	

2 *Good results* Forty-one patients or 30 per cent of the group have been placed in this category. These patients are much improved since operation and have remained so. They cannot be said to be completely symptom free, but their symptoms are quite easily kept under control. For the most part the residual symptoms are related to the reduced capacity of the stomach and the altered mechanics of gastric emptying rather than simulating the original symptoms. In Table XII an attempt has been made to analyze and classify these residual symptoms. This group of patients is the one most difficult accurately to appraise. The cases seem to fall conveniently into the following groups although some overlapping necessarily occurs: (a) patients who are not as strong as formerly. Inability to regain former strength is not infrequent and often is associated with failure to regain or maintain weight. These persons require more sleep along with regular hours of work and their physical endurance is somewhat below par. They often are more susceptible to upper respiratory tract infections, (b) patients who are entirely symptom free, but, because in the past they have become so accustomed to following a rigid ulcer diet, they now refuse to discontinue it for fear of further trouble. Some of these patients probably belong in the excellent group, (c) those whose

symptoms are due to the small capacity of the remaining stomach. These individuals are apt to experience discomfort after a heavy meal, from overeating or from eating too rapidly. Many of these symptoms improve gradually as the gastric pouch dilates, some patients never overcome them, (d) those who have symptoms of sweating, a sensation of warmth, cardiac palpitation and faintness and weakness after meals. These have been ascribed by Custer, Butt and Waugh<sup>13</sup> and others to the dumping syndrome and explained by the rapid entrance of food into the jejunum. It is common experience among roentgenologists to observe rapid emptying of the gastric remnant after subtotal resection whereas only a few patients experience this train of symptoms. Many patients with such symptoms in our experience exhibit definite evidence of spontaneous hyperinsulinism and are relieved by the use of a high protein, low carbohydrate diet, (e) patients who have specific food intolerances similar to those mentioned above but more severe and often necessitating a modified diet for control.

It is important to note that one-half of the patients in this group with residual symptoms have co-existing diseases quite capable of accounting for all or many of their complaints. Thus, three of the living patients have definite roentgen evidence of cholelithiasis and one whose complaint is severe weakness has recently been shown to have developed macrocytic anemia. One patient has bronzed diabetes. Two patients have died of carcinoma developing in the gastric remnant. Presumably their gastric symptoms which returned after several years of complete freedom were due to the new disease, as the microscopic examination of the original ulcers showed them to be benign. Another patient subsequently developed carcinoma of the colon from which he died and which probably explained his symptoms. Other lesions more difficult of evaluation and for the most part occurring singly are listed in Table XII. It is not surprising to find such associated disorders frequently in a group of patients such as these who are at or beyond middle age.

These results compare favorably with those of St. John Harvey Guis and Goodman<sup>14</sup> who reported 90 per cent of the survivors of operation as having satisfactory results when grouped according to cases and 92 per cent satisfactory years according to their methods of tabulation. Walters and Clagett<sup>15</sup> state that the results of the surgical treatment of chronic gastric ulcer are among the best in the field of surgery.

3 *Poor results* Seven patients or 5 per cent of the group have unsatisfactory or poor results not due to stomal ulcer. These are summarized in Table XIII. Four patients are living and three have died at 7 years 9 months, 11 years and 2 months and 18 years and 2 months respectively. Three women who had a conventional type of resection have continued to have the same symptoms following operation. Repeated attempts by various methods of examination have failed to reveal an anastomotic ulcer and the long time which has passed with no essential change in the clinical picture militates against this diagnosis. One of these patients was re-explored 12 years after the original operation for a suspected marginal ulcer, but only a small gastric polyp was

found and removed. Her symptoms remained unchanged. An adequate explanation of the poor results so similar in these three cases is difficult or impossible and perhaps relates to some underlying functional disorder in addition to the organic disease. One man who had a Finsterer type of resection remained in poor health until the time of his death by suicide seven years and nine months later. He was a frequent visitor at the hospital on the Neurology

TABLE XIII  
GASTRIC RESECTION FOR GASTRIC ULCER  
Analysis of Poor Results—7 Cases

No of Cases	Comment	
3 Classical operation	Persistence of original symptoms	1 died 18 yrs 2 mos 1 living 5 yrs 8 mos 1 living 3 yrs 10 mos
1 Finsterer operation	Organic brain disease—alcoholism	Died (suicide) 7 yrs 9 mos
1 Palliative gastrectomy	Reactivation of ulcer (hemorrhage)	Living 12 yrs 8 mos
1 Total gastrectomy	Severe post resection symptoms macrocytic anemia	Living 5 yrs 4 mos
1 Classical operation	Incisional hernia (intermittent obstruction)	Died 11 yrs 2 mos

service. An anastomotic ulcer was never demonstrated and due to his demented state, institutional care was required. The one patient upon whom a palliative gastrectomy was performed in our opinion has not had a satisfactory result.

He developed symptoms of reactivation of his unremoved ulcer two years postoperatively. Strict dietary and medical management have sufficed to hold the disease in check. Stomal ulcer in this case has been excluded to the best of our knowledge. One of the three patients who underwent total gastrectomy has a poor result in the form of severe post resection symptoms. He is a severe psychoneurotic, has pronounced hyperinsulinism and has recently developed macrocytic anemia. The final case in this group is listed here, in spite of an apparent cure of his ulcer due to the fact that a large incisional hernia developed after operation. Until the time of his death 11 years and two months later, he had symptoms of intermittent intestinal obstruction. He repeatedly refused to have the hernia repaired and while the clinical results in this case must necessarily be recorded as poor, it should not stand as an indictment against the operation as far as the ulcer results are concerned.

4 *Jejunal ulcer*. Jejunal ulcer, while of rare occurrence, following gastrointestinal anastomoses for gastric ulcer is a most serious and distressing complication when it occurs. Church and Hinton<sup>16, 17</sup> reported three marginal ulcers in nine cases of gastric ulcer treated by gastroenterostomy and a questionable recurrent ulcer in one case treated by resection. Heuer reported three cases in which a stomal ulcer following resection was suspected but not proven. There were four verified jejunal ulcers in the present series. The pertinent clinical data of these cases are epitomized in Table XIV.

The first case is an example of a patient who required multiple operations for repeatedly recurring marginal or jejunal ulcers. This man was operated upon three times for recurrences. The original lesion was a high lesser curvature ulcer and a fairly radical Polya resection was performed. The

# GASTRIC ULCER

antrum, however, was not removed. Apparently it was left for the sake of simplifying the operative procedure. Accordingly this patient should be regarded as one who did not have an adequate primary resection. Unfortunately at the subsequent operations the antrum and pylorus were not excised. The second case is very similar and in view of the evidence now available, it is quite certain that the Finsterer procedure should never be used when dealing with gastric ulcer. In addition to the fact that one-half of the end results of this operation were unsatisfactory it is noteworthy that none of the remaining cases were in the excellent group. The third case is one in which a type of Finsterer operation was probably performed although not intentionally. The

TABLE XIV  
JEJUNAL ULCER—4 CASES

Case	Recurrence	Subsequent Course
1 M 52—Posterior polya (Finsterer) 8-3-27	8 mos	(1) Reresection 9-26-28 (2) Closure of acute perforation (elsewhere) Dec 1937 (3) Exclusion of jejunal ulcer 8-12-38 (4) Died (cerebral hemorrhage) 1-5-39
2 M 55—Posterior Hoffmeister (Finsterer) 7-18-28	18 mos	(1) Exploratory and jejunostomy 11-6-30 (4) Died 11-28-30 No autopsy
3 M 61—Posterior Hoffmeister (Finsterer) 4-1-43	Immediately Gastrojejuno- colic fistula	(1) Resection duodenal stump 5-19-44 (2) Colostomy and jejunostomy 4-25-45 (3) Died 6-23-45 Autopsy—perforation-peritonitis
4 F 69—Posterior Hoffmeister 1-27-44	9 mos	(1) Reresection 5-17-46 (2) Died 5-18-46 Hemorrhage No autopsy

lesion was on the lesser curvature and associated with a good deal of inflammatory reaction. The lower transection is stated to have been "close to" the pylorus. Symptoms of a marginal ulcer occurred promptly and one year later it was thought advisable to resect the upper portion of the duodenal stump. McKittrick<sup>18</sup> and Marshall<sup>19</sup> have reported nine cases in which jejunal ulcers have healed following such an indirect attack. Interestingly enough histologic examination of this specimen revealed the presence of gastric mucosa, but unfortunately the ulcer was uninfluenced by the procedure and progressed to the stage of a gastrojejunocolic fistula. Later, perforation occurred with a resultant general peritonitis in spite of the fact that the fistula had been excluded by a proximal colostomy and a catheter jejunostomy for feeding purposes. The remaining case in this group is that of a woman of 69 who had a prepyloric ulcer. A conventional resection which was adequate according to all of the usual criteria was performed. One year later a jejunal ulcer was easily demonstrated roentgenographically. At this examination it was estimated that two-thirds of the stomach had been removed. Gastric acidity remained at about normal levels prior to reresection. It is conceivable in this case that antral tissue was left behind in the upper segment by removal of too little of the lesser curvature, and that a higher resection might have given a better result.



## WEIGHT CHANGES

The post resection changes in weight are given in Table XV. An attempt was made to compare the stabilized postoperative weights as attained several years after operation with those of the patients before the procedure. The pre-operative weight selected was the average or possibly the best past weight. The weight immediately before operation is a poor criterion as most of these patients had lost from 15 to 25 pounds during the several months prior to surgery and a comparison with this weight would show either little or no change or more probably a gain. It will be noted that after resection the average patient is nearly 12 pounds below his former weight. Rarely is the loss excessive or sufficient to cause concern. It may, however, be associated with loss of strength and in some cases this may become a difficult problem. An

TABLE XV  
POST RESECTION CHANGES IN WEIGHT—112 CASES

Change	No. of Cases	Range (Pounds)	Average (Pounds)
Loss	84(75%)	5-45	17
Gain	15(13%)	3-25	10
No change	13(12%)		

Overall average 11.7 pounds loss

interesting study of this matter has been made by Wollager, Comfort, Weir and Osterberg<sup>20</sup> who found that following the Polya type of resection nearly all persons lost more fat in the stool when taking a high fat diet than did those who had not had a gastric resection. This was also true in some patients who were on a diet of ordinary fat content. Moreover some patients after the Polya operation lost more nitrogen and total solids in the stool than did normal individuals. The authors conclude that the amounts of fat and nitrogen lost in the feces were not large, but unless a diet of sufficient caloric content to compensate for this loss is taken a decrease in body weight might be expected.

## SUMMARY

The end results of gastric resection for gastric ulcer as viewed over a 20-year period support the earlier impression that this is the best means now at our disposal for the treatment of those ulcer cases which require surgery. The operation has limitations and for patients who are exceedingly obese are poor risks or who have high or inaccessible lesions, a less ideal but safer procedure should be selected. With the advent of vagal interruption a new and potent method is available for this group of cases. It is also conceivable that, as suggested by Lahey,<sup>21</sup> subdiaphragmatic vagotomy may be worth while at the time of subtotal gastrectomy in an attempt to prevent jejunal ulcer in that small group of patients who may be expected to develop this complication even after an adequate resection. The conventional subtotal resection whereby a large portion of the lesser curvature as well as the antrum and pylorus were removed, has given the best results in this series. Little difference has been noted in the late results between those cases in which a Polya or a Hoffmeister

reconstruction was performed, and likewise the clinical results of cases of antecolic and retrocolic anastomoses were essentially the same

The Finsterer exclusion operation would seem to have no place in the treatment of gastric ulcer and in view of a better understanding of gastric physiology it should be abandoned. Palliative gastrectomy, as observed in one case, did not yield a satisfactory result and it would seem that today there are other and better methods of dealing with high gastric ulcers. The record of the three total gastrectomies is not good. Although there was one excellent result, there was one operative death and one poor result. The procedure seems much too radical for the treatment of a benign ulcer but for the type of case in which it was here employed any substitute operation must be one which includes removal of the ulcer. In general an operation with 92 per cent of satisfactory end results compares favorably with the results of almost any major surgical operation today. The operative mortality herein reported can most certainly be reduced in the future and by heeding some of the lessons learned from this study it is hoped that the unsatisfactory clinical results can be further reduced in number.

The fact that microscopical study revealed malignancy in 10 per cent of the lesions which was not recognized as such at the time of laparotomy would indicate that any indirect operation for gastric ulcer should be accepted with caution. We believe that there is a definite place for medical treatment in the management of certain gastric ulcers but that its dangers and limitations should be realized by internists as well as surgeons. The side-effects resulting from large gastric resections which occasionally occur in the form of post resection symptoms and nutritional disturbances are perhaps the most objectionable feature of the operation. Fortunately most patients experience but little inconvenience on this score, but as newer and better methods of treatment become available, it is to be hoped that all postoperative residual symptoms can be eliminated.

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DISCUSSION—DR ROSCOE R GRAHAM, Toronto Dr Ransom was good enough to make available the material in his paper prior to his address He has rightly stressed that the proper therapy in gastric ulcer is still predicated on our ability or lack of ability to differentiate a benign from a malignant ulcer It is noteworthy that in his series there was a 10 per cent error in considering as benign an ulcer which histologically was proven to be malignant In a series of our own cases the error was as high as 17 per cent Some years ago Dr Harold Wookey re-examined specimens in our museum which had been labelled as benign gastric ulcer More detailed histologic study showed that 18 per cent were malignant

Singleton and Summers reported on 309 patients suffering from pre-pyloric lesions, 189 were carcinoma and 120 were benign lesions It was interesting, however, that in 24 of the malignant cases the crater was the only index of abnormality and in 17, or 85 per cent of these the crater was less than 2.5 centimeters in diameter

In a follow-up series of gastric carcinoma, there were a few cases in which it was felt that the carcinoma had been grafted upon a previous chronic ulcer While these could have been controlled by earlier surgical excision of the ulcer, it was heartening to find that the prognosis in such a gastric carcinoma was better than in one which started primarily as a carcinoma

Previously we have withheld operation on patients suffering from gastric ulcer until our hand was forced In most instances we had not advised operation until there was involvement of contiguous structures in practically all cases This gave a definite mortality and a difficult technical problem With the data which Dr Ransom has presented, it becomes obvious that one should entertain very seriously the policy of advising early radical operative procedures for a patient with a gastric ulcer The present regimen of preoperative care for gastric patients enables a radical gastrectomy to be carried out

without a prohibitive mortality. We are therefore justified in advising patients suffering from what we believe to be a benign gastric ulcer to accept operation early in the course of the disease.

We believe that the operation should be a radical gastrectomy. We have never accepted the Finsterer type of operation, in which a portion of the pyloric antrum was left in situ, even though a radical resection of the stomach was done. It is our conviction that the pyloric mucosa should be removed in its entirety in cases of gastric resection for ulcer.

DR F B ST JOHN, New York. It is the type of report which Dr Ransom has just made, representing a careful study of 175 cases of gastric ulcer which have been treated by partial or subtotal gastrectomy, which brings out informative material and matters for further consideration. Following the cases carefully, as has been done in this series, is of course the outstanding factor in evaluating the results. One cannot help but be impressed in general by the very satisfactory results obtained in his clinic.

The paper also introduces the interesting group of cases in which carcinoma was either suspected or actually proven either at operation or later in the surgical pathologic laboratory.

Dr Harold D Harvey, an associate on the surgical staff of the Presbyterian Hospital in New York, and I are about to finish a review of some 400 cases of subtotal gastrectomy for duodenal and gastric ulcer in the last ten years. The results have been gratifying in that the cases without symptoms of any significance followed on an average of about four years, show that 85 per cent have had no trouble. If the cases that either died or were lost to follow-up are eliminated, it would be approximately 90 per cent. In following these cases, we record any one of them as unsatisfactory if at any time during the follow-up period symptoms of significance have appeared. The work will be published in the near future. We realize fully that subtotal gastrectomy is by no means the satisfactory answer to these chronic inflammatory lesions of the stomach and duodenum as an ultimate form of therapy.

In our follow-up clinic we do not speak of end results in the course of a follow-up period, as we prefer to follow our cases in continuity and no ulcer case is closed, so to speak, so that we are establishing records of greater longevity which eventually will be of greater value. Any student of this disease will appreciate the importance, I think, of this method of following cases.

A word about operative mortality during the ten-year period represented by this study. In our series it was 4.6 per cent, but of the 18 postoperative deaths 16 occurred in patients over the age of 45, the death rate for patients under 45 being between 1 and 2 per cent, whereas in the older age group it was about 7 per cent, and in this latter age group cancer had been suspected in almost half the cases. Hence the feeling that resection was indicated in any event.

Another interesting point in Dr Ransom's results is the fact that if one studies a large series of cases, such as in the past 20 years, it must needs include a number of limited partial gastrectomies, in the first decade especially, and it is well known that the results in this type of procedure are not as satisfactory.

DR FRANK H LAHEY, Boston. I do not wish to add anything concerning the matters particularly discussed in this paper, but to bring before this busy surgical audience one point, and that is, how are we going to make the decision in patients with gastric ulcers, in which case we should apply and continue medical treatment, in which not to, and on what basis? I am well qualified to speak on this subject, since I have promoted over the years a set of criteria for applying medical measures to patients with gastric ulcers which I would like now to relinquish publicly.

I have said over the years that if a patient with a gastric ulcer showed freedom from symptoms, the absence of occult blood in the stools, and if the lesion disappeared by roentgenologic examination, he could be treated medically. I would like to change this

position and state that I now believe that every patient with gastric ulcer should have a gastric resection, and for the following reasons. Our present mortality in the resection of 110 consecutive gastric ulcers is zero, compared with a mortality of 26 per cent in approximately 400 subtotal gastrectomies for duodenal ulcer and 22 per cent in approximately 100 consecutive subtotal gastrectomies for jejunal ulcer. I believe that all gastric ulcers should be resected because we have found it impossible in doubtful cases to be sure that patients come back often enough to be checked adequately against malignancy and too many of them, when they have returned because of distressing symptoms, have been found to have an inoperable malignancy. I believe that the situation with gastric malignancy is so depressing that, particularly when subtotal gastrectomy for gastric ulcer can be done with such a low mortality, enough early carcinomas will be discovered to make the operation worth while. I believe in any lesion in which the pathologist himself, unless he makes serial sections, is often unable to determine whether or not malignancy is present, that there are no methods by which surgeon, gastroenterologist or medical man can be sure that he is not carrying on medical treatment in one out of ten patients who may well have cancer of the stomach.

There is no question but that there will be some ulcers resected which could have been treated medically, but the fatality percentage in this group from subtotal gastrectomy will, in my opinion, be infinitely lower than would be the case if some of these patients were treated medically and the malignancy overlooked until any prospect of cure by surgery was lost.

DR HENRY K RANSOM, Ann Arbor, Mich (closing). I wish to thank Drs Graham, St John and Lahey for their comments. Dr St John mentioned some of the difficulties encountered in the follow-up work. This has been true especially in our group listed as "good" results. These patients have been relieved of their original complaints but have some residual symptoms of different sorts. On careful examination many are found to have other diseases such as gallstones, syphilis, heart disease, etc., which could account for some or all of their symptoms.

An evaluation of the results of surgical treatment must take into account the operative mortality. Our mortality for this series was 7.9 per cent. I am glad that Dr Lahey emphasized the point that at the present time this has fallen to a low level as evidenced by his excellent record of no deaths in a large group of cases.

One of the difficulties encountered after operation in certain patients is the syndrome sometimes referred to as the dumping stomach. These individuals experience a feeling of weakness, sweating and cardiac palpitation after meals. In certain of these cases we have found the condition of alimentary functional hyperinsulinism. The fasting blood sugar is normal but after the ingestion of glucose, the level at the end of the first hour rises far above the normal reading. This is presumably due to the rapid filling of the jejunum with chyme due to loss of the pyloric mechanism. In turn, an unusually rapid absorption of dextrose takes place. The high blood sugar then stimulates the normal islet cells of the pancreas to an excessive release of insulin which brings the blood sugar down to hypoglycemic levels at the end of the second or third hour. Thus, instead of being about 65 mg per cent at this time it is often as low as 35 or 40 mg per cent. This mechanism seems to offer a plausible explanation in some patients for the train of symptoms often referred to as the dumping syndrome. In our experience the best treatment consists in the use of a high-protein, low-carbohydrate diet.

# THE EFFECT OF VAGOTOMY ON HUMAN GASTRIC FUNCTION\*

## A Preliminary Report

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THE FIRST ATTEMPTS to treat peptic ulcer surgically by gastric denervation, produced results which were difficult to evaluate. These indifferent reports, the different kinds and degree of denervation attained, the lack of understanding of the rationale, and the failure to pursue the problem further, apparently caused the procedure of vagotomy for peptic ulcer to remain obscure<sup>1, 2, 3</sup>. In recent years, however, the procedure has been revived in a different light, based upon a better understanding of the physiology of the stomach and of the ultimate cause and mechanism by which peptic ulcer is produced<sup>4, 5, 6, 7, 8, 9</sup>. It is the opinion of many that the ultimate cause of the lesions is secondary to (1) alterations of psychogenic or neurogenic origin, (2) alterations of the functions of cells of internal or external secretion, (3) local alterations of the mucosal anatomy or physiology of the affected mucosa, or (4) a reduction of the constituents of gastric contents produced by other organs, viz., hepatic, duodenal, salivary, or pancreatic secretions. Likewise, it is generally believed that the mechanism of ulcer production is the proteolytic activity of the gastric contents versus the mucosal resistance to devitalization and ulceration.

With the revival of this neglected procedure, comes the repeatedly demonstrated observation that complete section of the vagus nerves to the stomach does permit rapid healing and prolongation of remission of benign peptic ulcer<sup>10, 11, 12, 13, 14</sup>. It is strongly felt that this favorable therapeutic response comes from an attack upon the mechanism of ulcer production, and more specifically, upon the proteolytic or peptic activity of the gastric contents. That continuous and prolonged reduction of peptic activity is necessary to obtain a therapeutic response is evident from the fact that if the ulcer is to heal, it must be given sufficient time. This healing time is achieved not by a temporary adequate reduction but by a sufficiently prolonged reduction of the peptic power of the gastric contents. Since peptic power is dependent upon products of gastric function, i.e., acid and pepsin, then the effect of vagotomy upon function could explain the therapeutic response.

The effect of complete parasympathetic denervation of the stomach is a lack of secretory and motor response to vagus stimulation, i.e., the cephalic phase is abolished. The response to humoral secretagogues, however, is not prevented by such denervation. The stimulation of intact vagi to the normal or ulcerated stomach produces a copious secretion of gastric juice high in proteolytic activity as well as an increase in gastric motility<sup>15, 16</sup>. The prevention

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of this stimulus to gastric function, therefore, would abolish the cephalic phase and the part it plays in the mechanism of ulceration. On the other hand, since gastric contents can be strongly proteolytic in the absence of vagus stimulation, it remains to be shown that a complete vagotomy will always produce a sufficient reduction in the peptic activity to permit an ulcer to heal or prevent its recurrence<sup>17, 18</sup>

#### PURPOSE

The purpose of this report is (1) to point out the fallacies of continuous gastric suction as a method for determining the volume of gastric secretion, (2) to describe briefly a new method for measuring the function of the human stomach, and (3) to present graphical data showing the usual response to some stimuli of the nervous and humoral phases of gastric function before and after vagotomy. The functions studied are (1) rate of secretion, (2) rate of emptying, (3) pH of secreted gastric contents, and (4) digestive power of secreted contents.

#### MATERIAL

The material studied consisted of 30 patients. Twenty-one were operated upon above the diaphragm, and nine below. Postoperative tests and clinical responses indicated that a complete vagotomy was achieved in each instance.

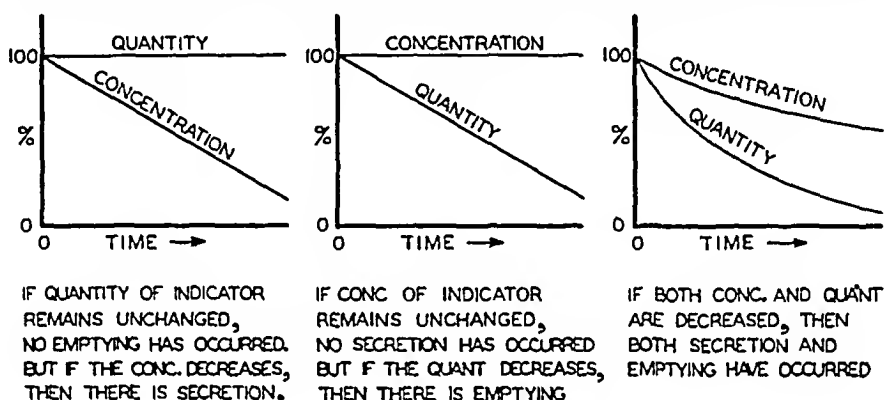
#### METHOD

A common method for measuring the volume of gastric secretion depends upon the complete recovery, by continuous suction on a stomach tube, of the total volume of juice secreted. This method is unsatisfactory because (1) a large portion of the secretion is emptied through the pylorus and therefore is not recoverable, (2) if any duodenal regurgitation occurs at any time during the period of continuous suction, it will be recovered in part and will increase the volume aspirated, (3) during a period of prolonged suction, or while the subject is asleep, saliva will also enter the stomach and be recovered, and finally (4) it is difficult to empty completely a stomach if the subject remains in one position during the period of aspiration.

The method employed in these studies for the quantitative determination of human gastric function has been reported elsewhere<sup>19</sup>. It consists of injecting into the empty stomach an isotonic solution containing a known amount and concentration of an indicator (phenol red), and after a 15-minute period aspirating the entire gastric residual contents. From the values of quantity and concentration of indicator injected and aspirated, can be calculated the average rates of gastric secretion and emptying during the test period. Evidence for the validity of the method has been obtained. Figure 1 is a simple graphical representation of the principles upon which the method is based. It is obvious that if the quantity of indicator in the stomach contents remains unchanged, no emptying has occurred. If the concentration decreases, then there is dilution of indicator by gastric secretion. From the middle graph, if the concentration of indicator remains unchanged, no secretion has occurred. But if the quantity decreases, then there is loss of indicator by emptying of

gastric contents through the pylorus. If both the concentration and quantity are decreased, then both secretion and emptying have occurred. The concentration of indicator injected and aspirated is determined by an electric colorimeter after precipitating proteins and bile, if any is present<sup>20</sup>. The volumes injected and aspirated are measured, and the quantity of indicator content is then calculated.  $C_0$  = indicator concentration of injected solution, and  $W_0$  = quantity (weight) of indicator injected.  $C_T$  and  $W_T$  are concentration and quantity at the end of a test period. Calculations of pH and peptic activity of secreted contents can readily be made.

#### RELATIONS BETWEEN SECRETION, EMPTYING & INDICATOR CONTENT



THE % REDUCTION OF INDICATOR CONCENTRATION AND QUANTITY PERMITS THE CALCULATION OF VOLUMES SECRETED AND EMPTIED VIZ.,

$$\text{VOLUME SECRETED} = \left[ \frac{W_0}{C_0} - \frac{W_T}{C_T} \right] \left[ \frac{\log \frac{W_T}{W_0}}{\log \frac{W_T C_0}{W_0 C_T}} - 1 \right] = S$$

$$\text{VOLUME EMPTIED} = \frac{W_0}{C_0} - \frac{W_T}{C_T} + S$$

FIG 1—Principles of Method for the quantitative determination of volumes of gastric secretion and emptying

#### RESULTS

The results of this study are represented by (1) data obtained from the same patient before and after vagotomy in response to nervous and humoral stimuli of gastric function, and (2) the average secretory response to insulin hypoglycemia (a potent stimulus to vagus function) in six subjects without vagotomy and in seven with vagotomy. Figure 2 shows the effect of the subcutaneous injection of 0.275 mg of histamine acid phosphate upon the secretory and emptying rates. Both secretory rates responded with an increase following the injection of histamine before and after vagotomy. This response is to be expected, because histamine is a humoral secretagogue and its action upon gastric function is independent of intact vagi. Before vagotomy, the increase of emptying rate in response to histamine may have been a consequence of a greater volume of gastric contents produced by the increased secretory rate. Figure 3 shows the effect upon the pH and peptic power of the secreted contents in response to the same drug. There was a marked



increase in the concentration of pepsin and hydrochloric acid (decrease of pH) before and after vagotomy. This response shows again that histamine acts independently of the vagus nerves. Notice the non-parallel relationship between curves of secretory rate and pH.

The response of gastric function to sham feeding before and after vagotomy is shown in Figure 4. The same subject chewed an orange during the period indicated without swallowing any of it. Preoperatively, there was an increase

#### SECRETORY & EMPTYING RATES IN RESPONSE TO HISTAMINE

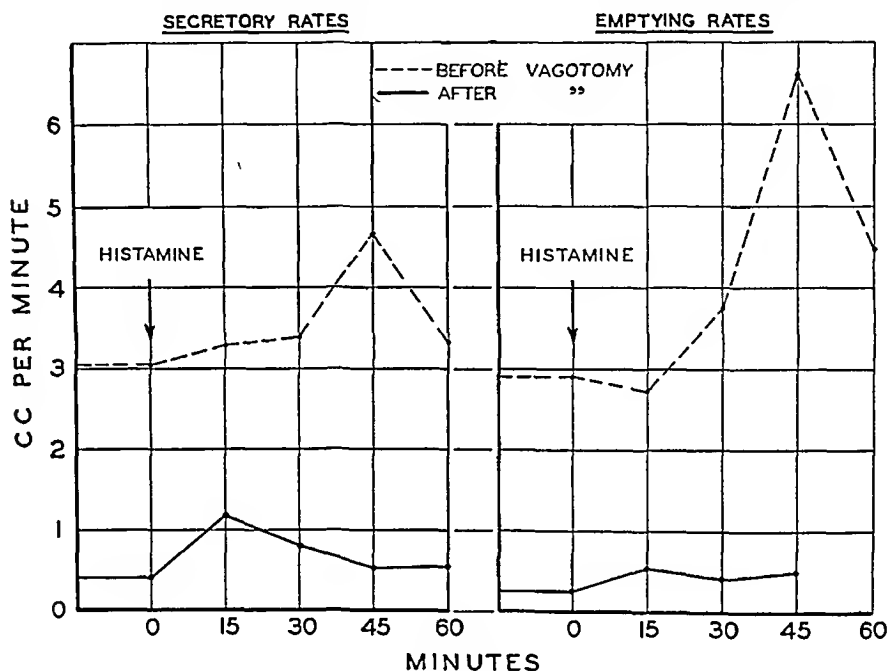


FIG 2—Patient J. S. Preoperative test done while patient had an active duodenal ulcer. Postoperative test 64 days after complete vagotomy with no evidence of ulceration. Note response to histamine and the marked reduction of pre-histamine (basal) rates after vagotomy.

in the secretory and emptying rates. Postoperatively there was no response following the sham feeding. These data demonstrate the absence of the cephalic phase of gastric function in a subject with vagotomy. Figure 5 shows the effect upon pH and peptic power of the secreted contents in response to the sham meal. Preoperatively there was a marked increase in the concentration of pepsin and hydrochloric acid after the feeding. Postoperatively, the pH remained unchanged, while the peptic power actually decreased. This again demonstrates the absence of the cephalic phase of gastric function in a subject with vagotomy.

A comparison of the control values (Fig 2, 3, 4, 5) reveals that all the functions studied were diminished postoperatively. There was a smaller percentage reduction in peptic power than in any of the other three functions. Emptying rates and acidity were most reduced. During the preoperative his-

tamine study, the subject had an active duodenal ulcer, and his control secretory rate was 3 cc per minute. At the time of the preoperative sham meal study, the ulcer was inactive and the control secretory rate was 1.2 cc per minute, showing that gastric secretion during exacerbation was two and one-half times the rate during remission. After vagotomy, the control secretory rate was only about 0.45 cc per minute which is but 15 per cent of the control rate at a time when the ulcer was active. This reduction of secretory rate is the goal of vagotomy, for with no cephalic phase of secretion, the entire burden

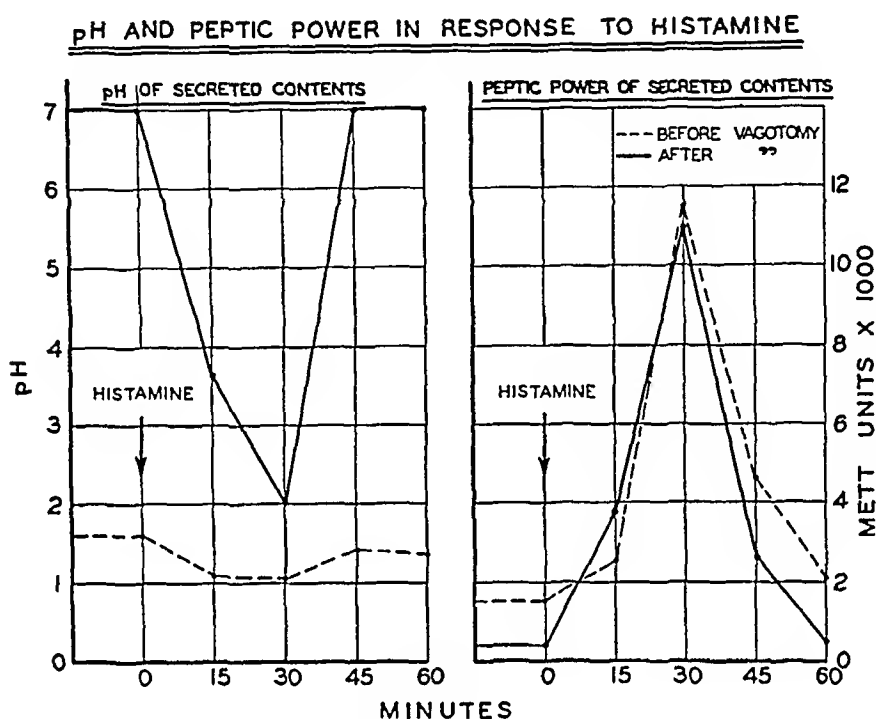


FIG 3—Patient J S Preoperative test done while patient had an active duodenal ulcer. Postoperative test 64 days after complete vagotomy with no evidence of ulceration. Note response to histamine and the reduction of prehistamine (basal) peptic power and acidity (increase of pH) after vagotomy.

of stimulating the production of sufficient hyperactive digestive juice rests with other secretory stimulants, *e g*, humoral secretagogues. In the majority of people these secretagogues apparently are not capable of stimulating the production of enough proteolytic juice of sufficient activity to produce or maintain a peptic ulcer.

Figure 6 shows the secretory response to insulin hypoglycemia before and after vagotomy. Seven tests were done on six subjects without vagotomy, and eight tests were done on seven subjects with vagotomy. This is unselected data and includes all tests done. In each person before vagotomy, the secretory rate was markedly increased after the injection of insulin. Whereas, postoperatively each person responded with a slight but definite decrease in the rate of gastric secretion following the injection of the drug. An explanation for this response is, that the hypoglycemia following the injection of enough

insulin strongly stimulates the vagus nuclei in the medulla. This in turn stimulates the intact vagus nerves to release acetylcholine at the synapse of the nerve endings with effector cells of the stomach. The acetylcholine then acts upon the secretory and motor cells to stimulate their activity, which results in the production of secretion and motility. It follows from this, that if the vagi to the stomach are severed, then the stimulus propagated along the nerve will never reach the stomach, and consequently there will be no increase of gastric function due to stimulation of these nerves by the hypoglycemia. These data indicate that the insulin test, when properly employed, appears as a satisfac-

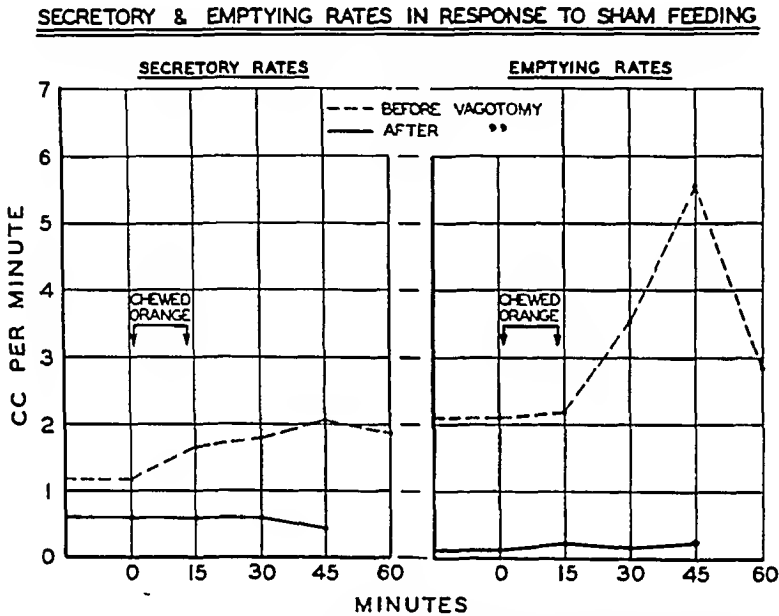


FIG 4—Patient J. S. Preoperative test done while patient was in remission from duodenal ulcer. Postoperative test done 64 days after complete vagotomy, with no evidence of ulceration. Note response to the sham-feeding and the reduction of pre-sham-meal (basal) rates after vagotomy.

tory means for determining whether or not the stomach has been sufficiently denervated.

In Figure 6 it can be seen that the average control secretory rate preoperatively was 3.25 and postoperatively 2.09 cc per minute. This represents a 36 per cent reduction of the average basal gastric secretion in response to vagotomy. However, it has been shown that there is no correlation between the rate of secretion and the concentration of pepsin or hydrochloric acid of the secreted contents. For example, in response to histamine there may be an increase in concentration of hydrochloric acid with no increase in total secretory rate. Therefore, it should be stressed that the volume of secretion produced *per se* gives no indication of the proteolytic power of the gastric contents. With this in mind, and again referring to Figure 6, it should be noted that the basal secretory rate in a person without vagotomy (note preoperative

pH AND PEPTIC POWER IN RESPONSE TO SHAM FEEDING

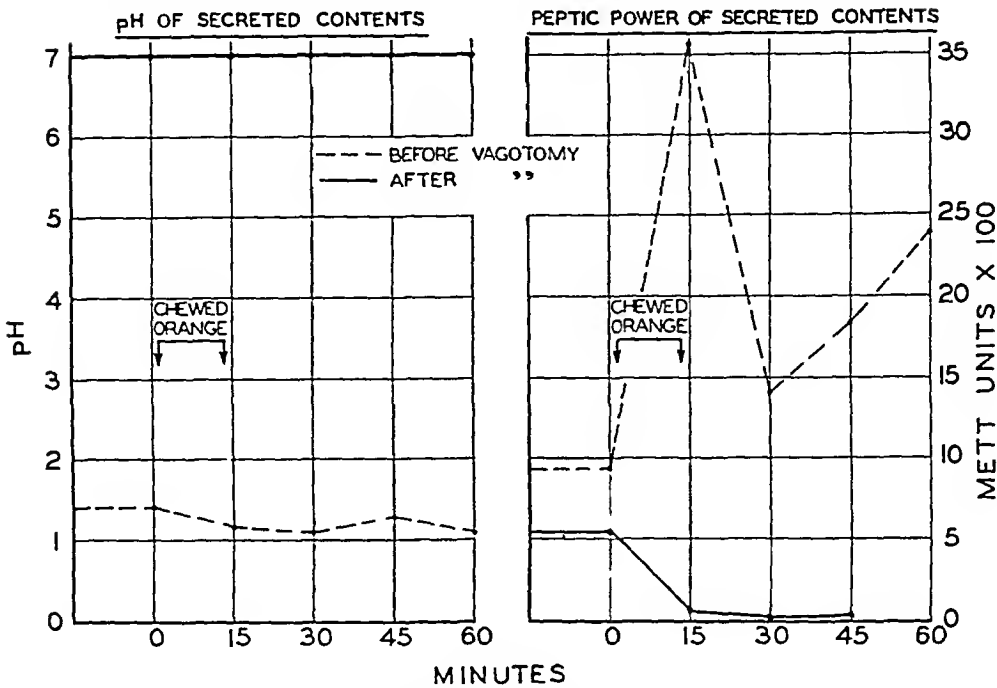


FIG 5—Patient J S Preoperative test done while patient was in remission from duodenal ulcer Postoperative test done 64 days after complete vagotomy with no evidence of ulceration Note response to the sham-feeding and the reduction of the pre-sham-meal (basal) peptic power and acidity (increase of pH) after vagotomy

SECRETORY RATES FOLLOWING INSULIN HYPOGLYCEMIA

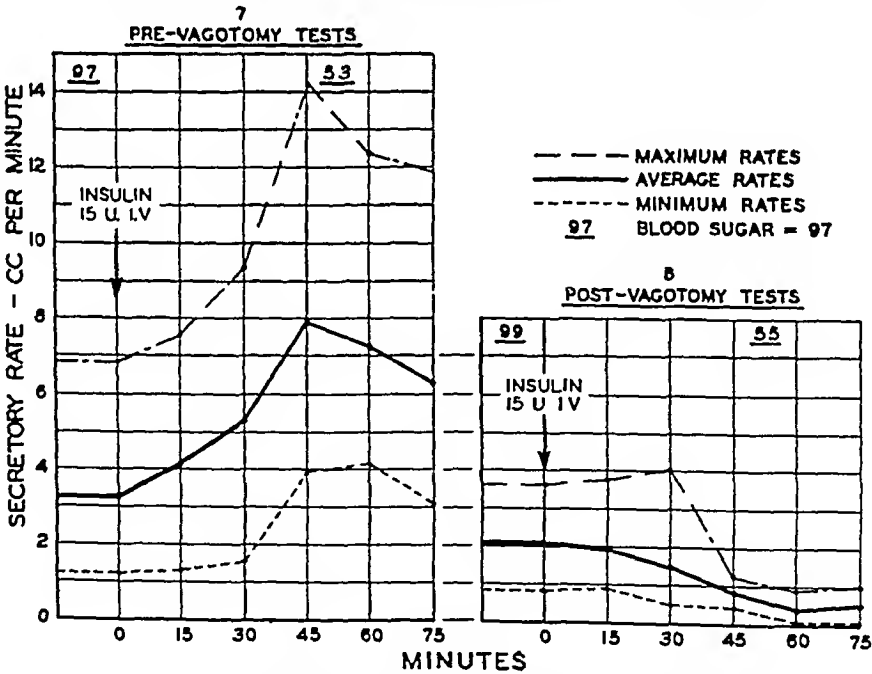


FIG 6—In each of the seven preoperative tests there was a marked increase in secretory rate in response to insulin hypoglycemia In each of the eight postoperative tests there was a reduction of secretory rate after injection of the drug Note that the average post-vagotomy pre-insulin (basal) rate was 36 per cent less than the average preoperative pre-insulin (basal) rate Also note that the maximum postoperative pre-insulin (basal) rate is higher than the minimum and average pre-vagotomy pre-insulin (basal) rates Solid lines represent the average of all tests Broken lines represent the maximum or minimum tests

control rate of minimum curve) may be considerably lower than the basal rate in another person with vagotomy (note postoperative control rate of maximum curve) The inference to be drawn from these comparisons is that preoperatively a low rate of basal secretion is no contraindication to vagotomy for peptic ulcer because the peptic power may be high And likewise, a high rate of basal secretion postoperatively is no criterion for incomplete vagotomy

## SUMMARY AND CONCLUSIONS

1 The mechanism for the production and maintenance of peptic ulcer is the proteolytic activity of the gastric contents versus the mucosal resistance to devitalization and ulceration

2 The fallacies of continuous gastric suction as a method for determining the volume of gastric secretion have been pointed out

3 A satisfactory method for the quantitative determination of human gastric function has been reviewed briefly

4 The gastric secretory response to histamine, a humoral secretagogue, is not prevented by complete vagotomy Therefore, a vagotomized stomach is still capable of producing active digestive juice

5 Complete vagotomy reduces gastric secretion and emptying by abolishing the cephalic phase of gastric function Peptic activity is least reduced

6 The basal secretory rate of six persons was reduced by an average of 36 per cent in response to vagotomy

7 In one person, the basal secretory rate fell from 3 cc per minute during a period of exacerbation of duodenal ulcer, to 1.2 cc per minute during remission In this same person, the rate was decreased to 0.45 cc per minute after vagotomy

8 The insulin test for complete vagotomy appears to be satisfactory when properly employed

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# VAGUS RESECTION FOR ULCER AN INTERIM EVALUATION\*

## II Clinical Results

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IN THE PREVIOUS PAP<sup>1</sup> of this series<sup>1</sup> the operative technic, postoperative management, and hospital morbidity and mortality of vagus resection for ulcer have been described. In this paper it is our purpose to present the clinical results in these patients two to 30 months postoperative.

### I CLINICAL DATA

The study of vagus resection at the Massachusetts General Hospital comprises at the present time a group of 84 patients who have had this operation performed. These patients divide themselves into two groups: 41 patients who were cared for on the charity wards of the Massachusetts General Hospital, and 43 patients from the private wards of the hospital who were under the care either of the author or of other members of the surgical staff.†

There are four patients in this group who have had vagus resection for diseases other than peptic ulcer. Six patients have been operated upon too recently to be of value in any consideration of clinical effects. The remaining 74 patients will form the subject of this discussion.

It is, of course, of no significance to use the term "end-result" in a study of ulcer therapy dating back only two and one-half years. Yet an appraisal of the present status of these patients is of the greatest necessity at this time.

The interim results in these patients have been evaluated by a careful clinical follow-up. In addition, within six weeks preceding the preparation of this manuscript, questionnaires were sent to all the patients. The return from these questionnaires included 97 per cent of the group. On the basis of these questionnaires plus the impressions of the physicians who have been following the patients, the clinical results have been ascertained. It should be emphasized that the questionnaire asked questions concerning the patient's ulcer pain, incisional pain, diarrhea, indigestion, and, in addition, gave the patient ample opportunity to express any further thoughts concerning the effects of the procedure on himself.

Follow-up x-rays have not been taken in all cases. This procedure has not been felt necessary unless the patient complained of an ulcer pain or had other disturbing symptoms. In three instances ulcer pain or bleeding occurred post-

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operatively, but by the time the patient was seen or admitted to the hospital all symptoms had receded and a negative x-ray has been of little significance in evaluating the symptomatic episode

Results from these cases have been classified into three categories

a *"Poor" Results* Patients have been adjudged to have a poor result if they had a frank recurrence of the ulcer, if they had ulcer pain or bleeding symptoms, or both. The classification of poor results may be considered in essence to include cases which have shown some evidence of recurrence, although at the actual time they were surveyed, they may not have had such symptoms

b *"Fair" Results* Fair results have included those patients in whom some postoperative event occurred which detracted very materially from any benefit conferred by the operation. In most instances, these difficulties disappeared within a short time, and the final result was satisfactory to the patient, yet the presence of transient major difficulties would prevent the result from being classified as good. In a few patients having "fair" results the final result at the time of this writing is unsatisfactory to the patient or to the physician, although the ulcer has remained healed

c *"Good" Results* Results are classified as good if the patient himself is satisfied with the result of the operation, if he has maintained himself free from symptoms without diet, and if the gastro-intestinal side-effects of the operation were not significant enough to cause him discomfort during more than a normal period of convalescence such as one might experience after any operation

This grouping arises in part from the viewpoint of the patient, in the final analysis the only person able to judge the symptomatic result in a disease the course of which over many years may be benign

This grouping of cases according to clinical result is shown in Figures 1, 2, 3, and 4. Of the 74 cases, 87 per cent have a result satisfactory by the most rigid criteria

Among the "poor" results is included a patient who had a retained gastric antrum removed before he became well<sup>1, 2</sup>. This patient is now well and at work. The case of recurrent ulcer with bronchogenic carcinoma is enigmatic. The patient is asymptomatic, whereas, before vagus resection symptoms were very severe. His duodenal ulcer is present by x-ray only. He has had a total pneumonectomy and the state of his duodenum, when he has recovered from this difficulty, will constitute the significant interim result. The other three patients in the "poor" result group have had ulcer symptoms eight to 30 months postoperatively and must be considered as failures, at least at this point. Their future course will be cause for considerable interest and concern.

The 13 patients with "fair" results may be grouped according to the satisfaction of the patient with the present state of affairs. Eight of the 13 are at present satisfied, though their course has been marred by undesirable events as shown in Figure 4. Five of these patients have had so much difficulty



with side-effects that their result must be judged unsatisfactory by any standards. It is of interest that some patients regarded as having unsatisfactory results in a previous report<sup>2</sup> have now cleared up their troubles and are well, at work, and satisfied. This intermediate classification is, therefore, a shifting one, it represents the status of patients at this phase of their convalescence and may increase or decrease in importance as time goes on.

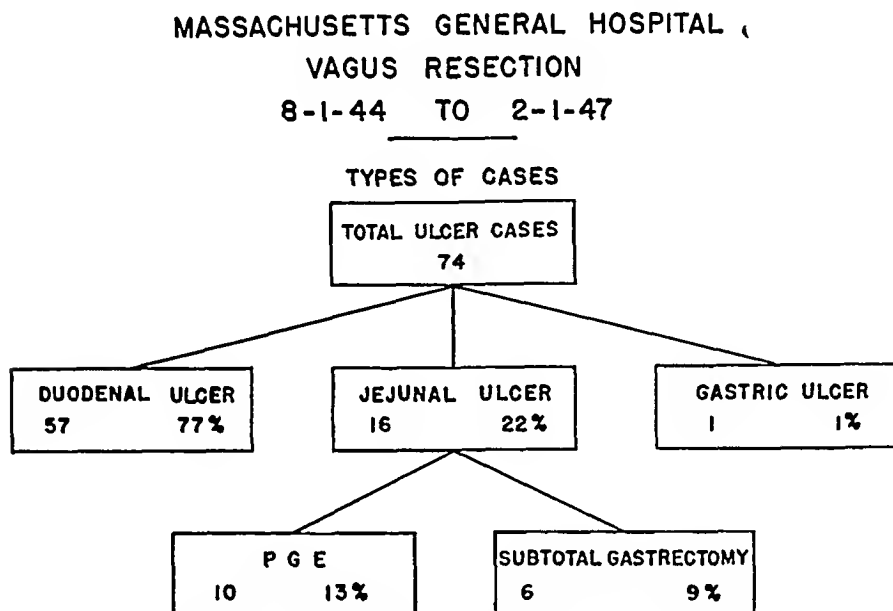


FIG 1—Types of ulcer cases treated by vagus resection

The histories of a few patients who are classified as having “fair” or “poor” results may be helpful in understanding what is meant by these classifications.

#### CASE REPORTS

**Case 1**—M G H Unit #390253. This patient first presented himself at the hospital three years ago at the age of 22. He was studied in the Out Patient Department because of the presence of ulcer symptoms and a demonstrable duodenal ulcer by x-ray. In July of 1945 the patient was admitted to the hospital because of intractability of his symptoms. It was found that there were many factors in this patient's background conducive to conflict, environmental and psychologic factors which might well be of considerable importance. Because of his lack of obstruction and the presence of an active ulcer, he was considered a good patient for vagus resection. However, the Psychiatric Service felt they might be able to help the patient and for that reason he was admitted to the Psychiatric Service and treated intensively for approximately three weeks. At the end of this time he had healed his ulcer and the patient was symptom-free.

Following discharge, the patient remained well for a month and one-half, at which time, having returned to the situation at home in which there were many difficult social and financial factors, the patient's ulcer pain returned. The patient noticed that his pain was made worse by worry, spices, or rich food. He noticed slight red blood in his stools on several occasions, although he never had massive hemorrhages. Barium enema was negative. It was decided at this time that he should have a vagus resection and on 12-6-45 he had a transthoracic transdiaphragmatic vagus resection.

VAGUS RESECTION

The patient's immediate postoperative course was marred by a transient episode of vomiting on the 9th postoperative day, possibly the result of advancing his diet too rapidly. However, he recovered from this and was discharged on the 16th postoperative day. X-rays at the time of discharge showed atony of the stomach and duodenum up to the ligament of Treitz in a fashion seen in other cases. The pylorus was not abnormally "spastic."

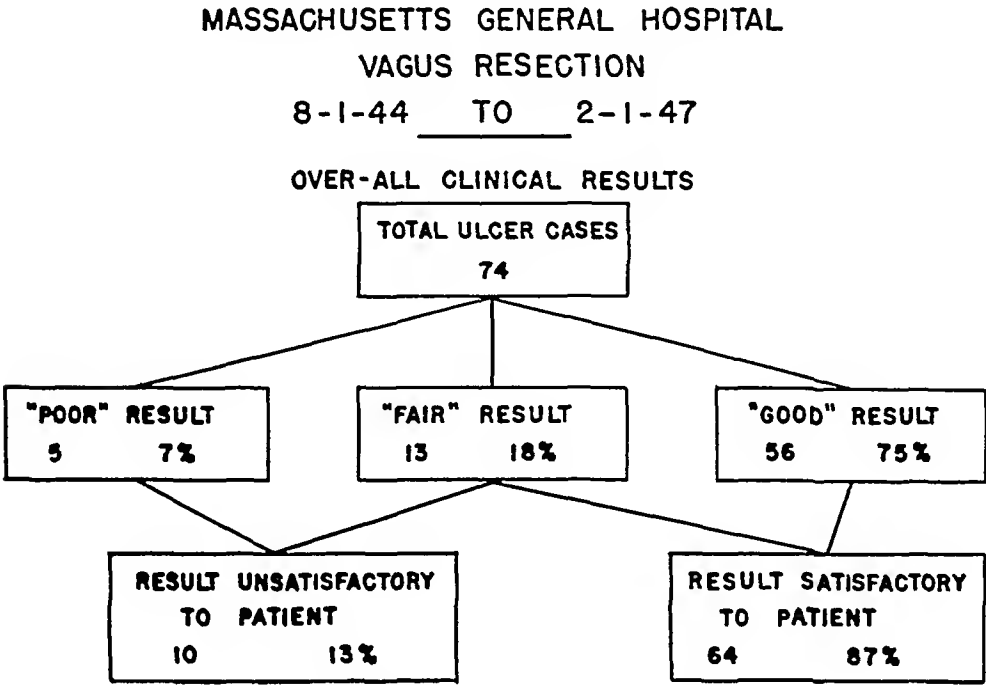


FIG 2—Overall clinical results

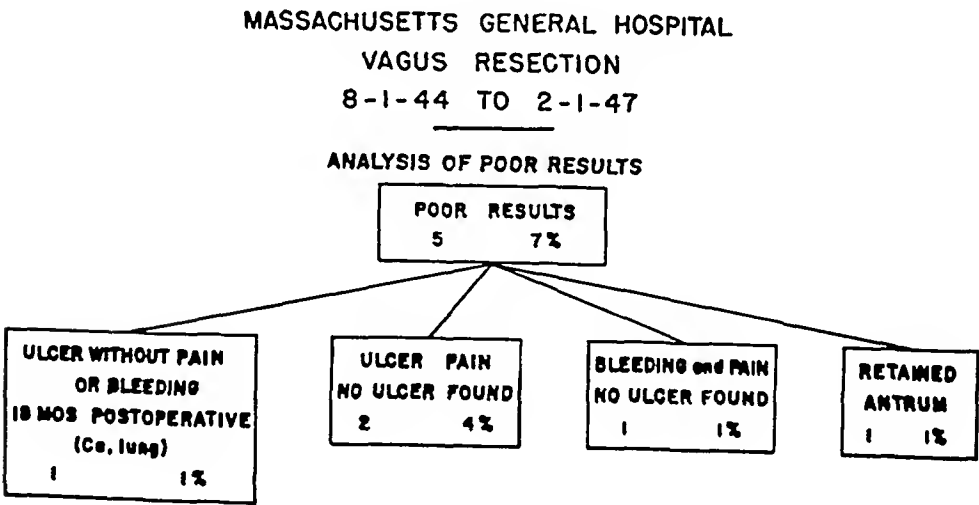


FIG 3—Analysis of "Poor" results

Two days before leaving the hospital, but unbeknownst to his doctors, the patient began to develop diarrhea and for approximately four months the patient had an extremely intractable diarrhea, possibly the most severe diarrhea seen in this series. However, despite this diarrhea, he gained five pounds during this time and did not show gross disorders of his plasma chloride or nutritional disturbances. At the time his diarrhea was disappearing, he was re-x-rayed and still showed striking motility disorders in the stomach.

He was re-admitted to the hospital in May of 1946 for routine re-evaluation. At this

time his ulcer was still healed, the gastric picture was returning to normal by x-ray and he was gaining somewhat more weight. In September and November of 1946 he was seen in the clinic and each time showed some weight gain, but he had begun to have occasional "ulcer pains." He stated that they were mild and like hunger sensations. He had also noticed that under certain circumstances he had discrete short bouts of diarrhea again. However, he was at that time fairly well satisfied.

This patient's general comments on his recent questionnaire may cast some light on his problem. "Whether or not the operation was a success, I cannot say for sure. During the last month and one-half I have had much pain. Why is it that these pains come back? I have had to give up a very good position because of physical inability to do the work. My weight has not improved to any great degree. The more I think of things which are bothering me, the more I get pain. Even if I eat right away, the pain abates, but does not go away."

Here, then is a patient who must be classed as a "*poor*" result because of the return of pain which is similar to ulcer pain and who, in addition, had very disturbing diarrhea for a four-month period. In retrospect, the patient tends to discount the diarrhea, but regards his present pain as a major factor. His repeat x-rays for question of recurrence fail to reveal an ulcer crater.

**Case 2**—M G H Unit #479283. A 41-year-old patient who first presented himself at the hospital on 2 12 45 with a diagnosis of jejunal ulcer. The patient had a long and complicated ulcer history, including the performance of a posterior gastro-enterostomy which was later taken down and replaced in 1939 by an anterior gastroenterostomy. At the time of admission he had a large jejunal ulcer and was operated upon 2 26 45 at which time a vagus resection was carried out. The patient was discharged on the 11th post-operative day, completely relieved of his symptoms and remained an excellent clinical result until June of 1946, approximately 15 months postoperatively. Throughout this period the patient reported frequently to clinic, re-entered the hospital twice for routine kymographic and acidity studies and remained one of the dramatic results in the series. In June of 1946 the patient overimbibed alcoholic beverages and was admitted to another hospital with acute hemorrhage from the gastro-intestinal tract which subsided quickly on therapy and bed rest. The bleeding was not massive and the patient was never in shock. He signed out against advice from the other hospital and returned to our care on 1 2 47 for study. At this point he was approximately 21 months postoperative. He was well at this time, had no symptoms of ulcer. He had no jejunal ulcer by x-ray, though there was one area of slight stiffening of the jejunum. The patient had an inguinal herniorrhaphy at this time, was followed in the clinic and has remained well.

This patient remains a good result as far as the patient himself is concerned. He must be included in the "*poor*" results because he had an episode of bleeding which was presumably due to ulcer. This emphasizes the critical nature of this classification. We must presume him to have had difficulty with ulceration unless definitely proven otherwise.

**Case 3**—M G H Unit #433311. A 42-year-old patient who first presented herself at the hospital on 1 11 44 with the diagnosis of Raynaud's disease, hiatus hernia, esophageal ulcer and duodenal ulcer. This complicated situation was treated by vagus resection carried out 8 4 44. She was the second patient to be operated on at this hospital by vagus resection. Vagus resection was chosen because it was felt that it might control both the esophageal and duodenal ulcers, although all concerned realized that a new operation was being applied to a rather complex situation.

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The patient's postoperative course was good for the first few months. However, after this time the patient began to complain of intermittent symptoms of fulness and had the symptom of regurgitation up her esophagus which bothered her tremendously. She returned to the hospital on 4 16 45 because of diarrhea and abdominal cramps. At this time obstruction to the outlet of the stomach was not striking and while in the hospital the patient's gastro-intestinal symptoms were mild. However, her Raynaud's disease was bothering her considerably so bilateral dorsal sympathectomies were carried out. Following this the patient was seen in the clinic and had a variable clinical course. X-rays taken at one point showed a recurrence of the esophageal ulcer, at a later occasion this could not be found. No clearcut recurrence of the duodenal ulcer was ever found, though in January of 1947, approximately 30 months postoperatively, the patient was very ill at home with a bout of vomiting which, in one day, changed from coffee grounds to bright red blood, with difficulty in swallowing. This picture passed off spontaneously in about one week, at the end of which time the patient came to the hospital, x-rays were taken, again no ulcer could be found, and there was no significant obstruction.

This is a patient whose checkered career postoperatively and the presumed recurrence of ulcer with bleeding makes it necessary to include her in the "poor" result group. Not only is she a poor result from the standpoint of the physician, but she herself is poorly satisfied with the results of her surgery. In retrospect, it is probable that a subtotal gastrectomy might have given her a better result, though some of her esophageal symptoms might have persisted even under those circumstances.

**Case 4—M G H Unit #502947** A 31-year-old patient first admitted to the hospital on 9 5 45 with a five-year story of duodenal ulcer with some symptoms of vomiting, treated unsuccessfully by an internist, with periods of hospital management. Vagus resection was carried out on 9 20 45 and the patient left the hospital on the 9th postoperative day, having had an exceptionally smooth course, taking a satisfactory diet. On 2 22 46, approximately five months postoperatively, the patient returned to the hospital because of vomiting and a presumptive diagnosis of pyloric obstruction was made. However, x-ray showed that obstruction was not at the pylorus but instead in the third portion of the duodenum at the point where the mesenteric vessels crossed the bowel. The duodenum, up to this point was quite widely dilated. The patient did well while he was in the hospital, took satisfactory diet without vomiting, returned home and was well for three more months until 5 11 46 when he returned with the same syndrome, both symptomatically and by x-ray. Treatment with acetyl beta methyl choline was unavailing and, therefore, on 5 17 46 a posterior gastroenterostomy was carried out, since which time the patient has been well, at work, gaining weight, and satisfied with the result.

This patient is included in the "fair" results, in the subgroup of those in which the final result is satisfactory to the patient. He cannot be considered a good result because of the development of symptoms which required additional surgery. His present status is satisfactory.

**Case 5—M G H Unit #344702** This patient was first seen in this hospital in 1942 at the age of 42 with duodenal ulcer and a colloid goiter. She had a subtotal thyroidectomy with an uneventful convalescence. In 1946 she again entered the hospital with duodenal ulcer this time complicated by uterine bleeding of unknown source. At this point it was noted that her ulcer had not done well on medical treatment. She was treated for her endocrine difficulty and given a six-meal bland diet and creamalin for her ulcer pain. She was re-admitted four months later in July of 1946 with still further bleeding and intensification of her ulcer pain. Because of the fact that her uterine bleeding had not

been controlled by endocrine therapy, a total hysterectomy was carried out. Her ulcer pain continued as an extremely intractable type of symptom. It was noted that her ulcer symptoms were related to the deplorable situation of her home affairs and in her marital relationships. As a personality, the patient appeared to be mildly psychoneurotic, most strikingly so when she was having severe pain. At times when she was free of pain she was pleasant and agreeable, and seemed to have a rather good insight into the nature of her difficulties. On 8-15-46 a transthoracic transdiaphragmatic vagus resection was carried out. The patient showed no difficulty in getting up to a proper diet. An x-ray 12 days postoperatively showed typical changes in gastric motility, but were otherwise not remarkable. She began to have diarrhea at the time she left the hospital, but she had been free of pain throughout her short postoperative course.

She was re-admitted to the hospital, however, about one week later because of a severe exacerbation of her diarrhea, up to 12 to 14 movements a day. She was treated with belladonna and tincture of opium as well as a constipating type of diet, and improved to some extent, so that two months later she was having only one or two bowel movements a day but still had a "nervous feeling" in her stomach.

The answers to her questionnaire indicated that she had had some ulcer pain postoperatively whenever she took medicine for her diarrhea. Her chest pain was a minimal factor. She had feelings of indigestion and fullness with gas and belching. She had no vomiting. She regarded these symptoms as a major factor and deterrent to the effect of the operation. Her diarrhea remained a problem which came and went, apparently related to emotional strain. She also had trouble sleeping at night. She stated that although her ulcer pain was better since the operation, the other symptoms which she had acquired constituted a serious disturbance.

This is a patient in whom the gastro-intestinal side-effects of the operation constituted a major drawback to her operative result and in whom only a "fair" result can be claimed.

## 2 SIDE-EFFECTS OF THE OPERATION

a *Diarrhea* The most common gastro-intestinal side effect of this operation is diarrhea. We did not realize the frequency of this symptom until the present questionnaires were sent to the patients. Many patients have diarrhea of such a minor and transient sort that they do not remember to mention it at their office or clinic visits. However, in filling out a questionnaire in which there were several questions concerning diarrhea, it was of interest to observe that over half of the patients who have had vagus resection have had significant diarrhea at some time or other during their postoperative career. There is no clear-cut correlation between the presence of diarrhea and the presence or absence of a gastro-jejunal stoma. It has been our experience that the diarrhea is usually associated with poor gastric emptying. One rather dramatic instance showed up the relationship between these two. This is a patient who had a dilatation of the stomach postoperatively. At the time his gastric dilatation disappeared the patient stated that his stomach felt better and that he was "putting things through." These feelings were associated with a striking decrease in his gastric residual. On the same day that his stomach began to empty he began to have diarrhea—six or seven movements a day—which lasted for four or five days. Many other patients have given the story that at the time they have diarrhea, they also feel distended, may have pain in the tip of the left shoulder, indicating diaphragmatic irritation, and often tell

## VAGUS RESECTION

of the eructation of offensive-smelling material. This would suggest that the diarrhea is a colonic manifestation of intermittent gastric emptying interspersed with periods of gastric stasis. Evidence indicating that in some cases it may be an "ulcer-equivalent" is presented below.

All these facts taken together might lead one to expect that performing posterior gastro-enterostomy in these patients would lessen the incidence of diarrhea, or that the pre-existing presence of a gastro-jejunostomy would decrease the incidence of diarrhea. However, this is not the case. The 19 patients in our series who have had pre-existent or concomitant jejunal stoma

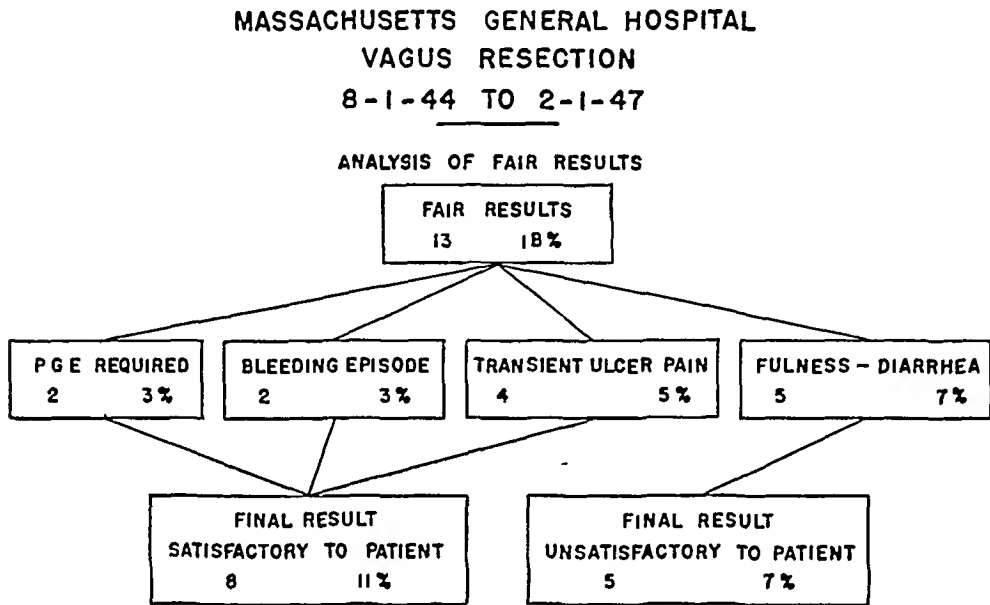


FIG 4—Analysis of "Fair" results

have had as much diarrhea as the others and in many cases suffered the same epigastric distention and sensation accompanying the diarrhea, as shown in Figure 5.

In evaluating diarrhea from the patient's point of view, one may divide the phenomena into three categories:

1 Minor transient diarrhea which is referred to by the patient as "of no consequence" (48 per cent of the cases)

2 Diarrhea which constituted at some point a major problem but which disappeared or was diminishing at the time the patient was surveyed (8 per cent of cases)

3 Diarrhea which constituted a major problem, a symptom as important to the patient as his ulcer and whose presence detracted in a major way from the result of the operation, (6 per cent of cases). Figures based on this classification are shown in Figure 6.

b *Emptying Disorders* The next common disorder of the gastrointestinal tract found in these patients may be described as "fulness." This symptom may consist of either a mild feeling of discomfort after eating a heavy meal, as is so commonly experienced in patients who have had a subtotal

gastrectomy, or frequent eructation (often of foul-smelling material), pain in the left shoulder or, in one or two cases, actual visible epigastric bulging. This is in every way a less significant symptom than diarrhea and in most patients was taken as a matter of course, and was transient.

Here again, these symptoms may be divided into three grades

- 1 Transient fulness (56 per cent of cases)
- 2 Fulness and eructation continuing and still bothering the patient (5 per cent of cases)
- 3 Fulness with vomiting, constituting a major problem detracting from the end-result of the operation (8 per cent of cases)

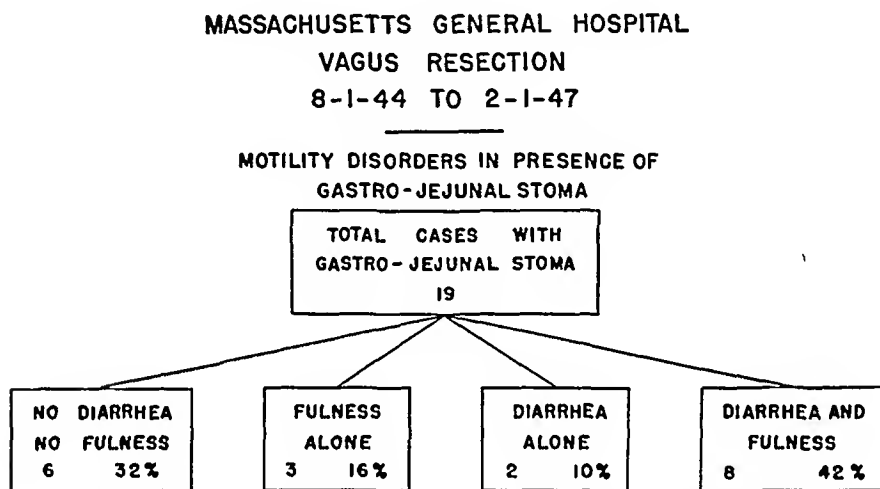


FIG 5—Motility disorders in the presence of a gastro-jejunal stoma

Figure 7 shows classification based on the above. As in the case of diarrhea, a gastrojejunal stoma is no solution to the difficulty, as shown in Figure 5.

c *Wound Pain* The third category of difficulties which may be experienced by patients who have had this operation is pain in the chest incision. One must recall that most major thoracic surgery is done for malignant disease or crippling cardiac or pulmonary disease in which incisional pain recedes into the background as a minor side-effect. In a patient with duodenal ulcer, especially if it has been a painless ulcer which has bled in the past, any sort of discomfort or pain is magnified in the patient's mind and becomes a major problem. The situation is analogous in every way to the incisional pain experienced by patients with hypertension. It must be regarded in a very different light from the incisional pain of patients who have been operated on for cancer.

In this series of patients incisional pain of a major sort was extremely rare. This is a series of cases operated on almost wholly by the thoracic route. In all of the transthoracic operations the rib was resected. There were no intercostal incisions. In the questionnaire sent to the patients, full opportunity was given them to express their thoughts concerning incisional pain. They

# VAGUS RESECTION

were quite frank in expressing their reactions relative to diarrhea and other side-effects of the operation, and there is every reason to believe that they would be frank and straightforward in their comments about the incision. It is therefore, of interest and significance to find that only two of the entire group stated that incisional pain had ever bothered them more than to a very minor extent (Fig 8)

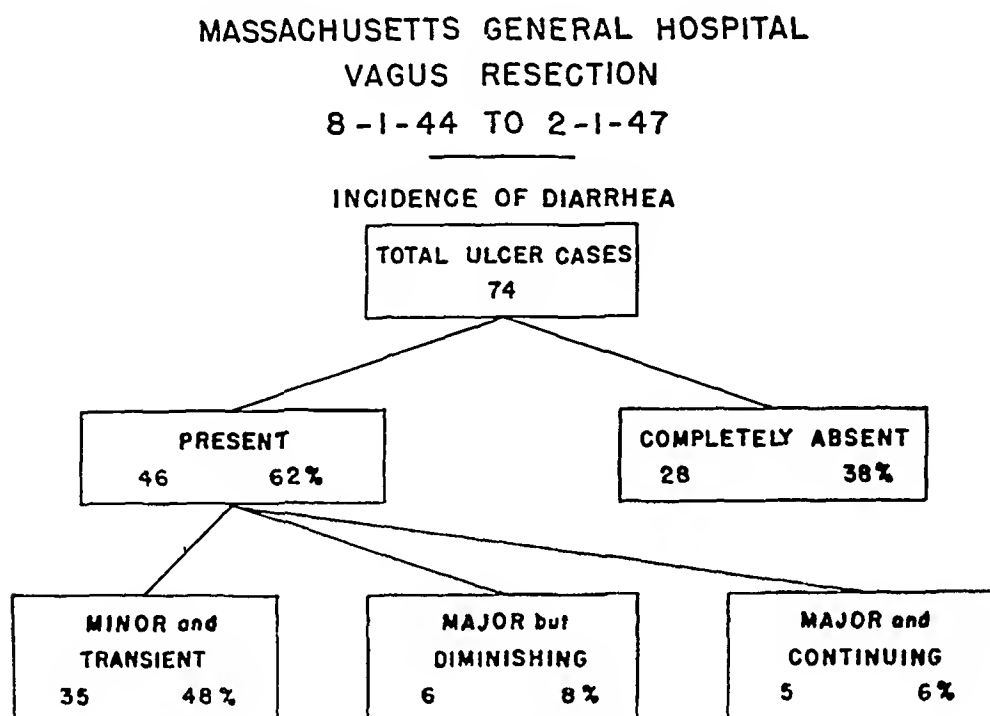


FIG 6—Incidence of diarrhea

Early ambulation and early motion of the arm are of importance in avoiding incisional pain. If the arm is splinted or put in a sling, or if the patient is allowed to favor it excessively for several days, a stiffness and immobility of the shoulder joint ensues which is often the source of considerable discomfort weeks or months later.

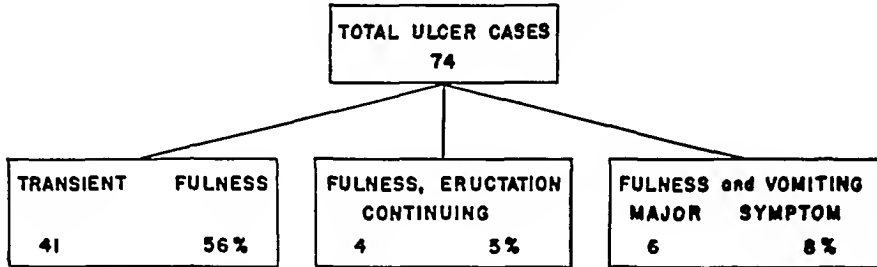
*d Miscellaneous Symptoms* There is one type of symptom experienced by patients who have had this operation which is of interest though it is rarely very bothersome to the patients, it is a symptom concerning which future research might be rewarding. This is a symptom which we have termed "nervous loading." It consists of a feeling of nervousness and of unspent nervous energy of an uncomfortable sort which the patient experiences at times when previously his ulcer would have bothered him. Having observed such symptoms, the author questioned many of his patients as to whether or not they had observed "ulcer-equivalents" in their postoperative activities. Two patients stated that the distention-diarrhea syndrome was a clear-cut "ulcer-equivalent" in their case. When they found themselves in a situation which formerly had produced epigastric burning and ulcer symptoms, they now noticed epigastric fulness and mild diarrhea.



The suggestion may be made that vagus resection, by "damming up" one source of cholinergic outflow from the midbrain, may produce some other disease in its stead. Candidates for such diseases, that have been mentioned,

**MASSACHUSETTS GENERAL HOSPITAL  
VAGUS RESECTION  
8-1-44 TO 2-1-47**

**INCIDENCE OF EMPTYING DISORDERS**



NO EMPTYING DISORDER CLINICALLY - 23 CASES 31% OF GROUP  
POST-VAGUS P G E NECESSARY - 2 CASES 27% OF GROUP

FIG 7—Incidence of emptying disorders

**MASSACHUSETTS GENERAL HOSPITAL  
VAGUS RESECTION  
8-1-44 TO 2-1-47**

**INCIDENCE OF INCISIONAL PAIN**

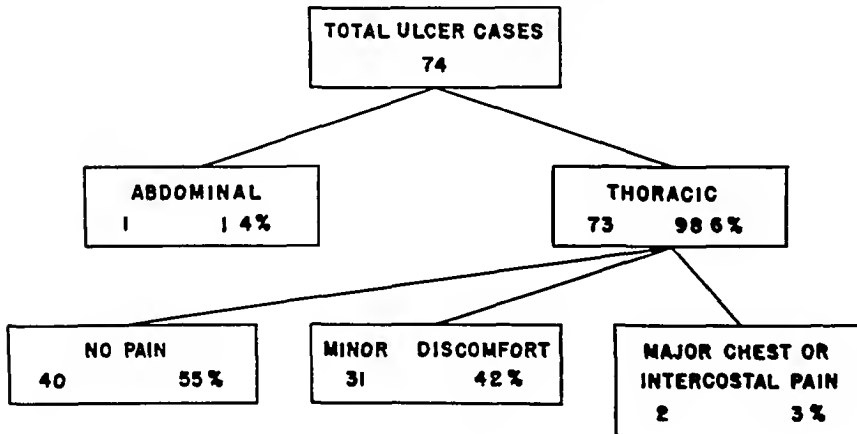


FIG 8—Incidence of incisional pain

are ulcerative colitis, bronchial asthma, thyrotoxicosis, and other so-called psychosomatic diseases. To date none of these diseases has developed, yet the "nervous loading" symptoms may be an expression of the outflow of pent-up emotional energy which previously found its vent in the ulcer syndrome.

### 3. DISCUSSION

Vagus resection for ulcer is at the crossroads. That it is an effective weapon in dealing with ulcer is well known. We now know the approximate magnitude of its side-effects, if not of its failures. From this time forward we must try to balance its significant advantages against its shortcomings so that we may arrive at an evaluation of lasting significance.

The enigma involved in evaluating this operation is best illustrated by the comments of patients themselves. Some of the patients are admirably satisfied by this apparently simple and physiologic solution to their difficulties. Other patients have had a great deal of trouble from side-effects and would lead one to adverse conclusions. Possibly at the risk of introducing unscientific, though colorful material, we might quote a few of the comments which patients have made in association with their questionnaires.

M G H Unit #454977 Male, age 36, duodenal ulcer 30 months postoperative

"I have never felt better than I have for the last two years. I have even enjoyed my food, worked as hard as ever and I have had no pain at all."

M G H Unit #480224 Male, age 62, jejunal ulcer 22 months postoperative

"So far the operation shows signs of being successful. I get pains in my back now and then, but not to any great account. I am able to eat anything without any distress."

M G H Unit #488327 Male, age 55, duodenal ulcer, 20 months postoperative

"I am bothered with gas under the scar on the right side. I take one teaspoonful of powder after my breakfast and supper."

M G H Unit #381380 Male, age 41, duodenal ulcer 18 months postoperative

"Considering the agonizing pains previous to the operation, I now feel the operation of vagus resection for ulcer is a great feat."

M G H Unit #501746 Male, age 38, jejunal ulcer 16 months postoperative

"The only thing I can complain about is gas. Sometimes after I eat I have a feeling of fullness, discomfort, and vomiting. If I cut down on my meals, I find I will not be so apt to have it. My general health has been very, very good and I am certainly free from ulcer pain."

M G H Unit #193174 Male, age 31, duodenal ulcer 12 months postoperative

"For about three or four weeks after the operation I had trouble swallowing food. It always felt as though I swallowed wrong, but that condition disappeared. For about nine months I had a pain in the left side of my neck. I now weigh around 148 pounds as to 135 before. I eat everything, drink anything with no ill effects."

M G H Unit #488323 Male, age 35, duodenal ulcer 12 months postoperative

"For about three weeks after I came home I had the diarrhea. Our family doctor gave me two different kinds of medicine, the name of which I don't recall. It took about three weeks before it stopped. It was so bad that water would go right through me. Then when that stopped, I started vomiting about once a day, sometimes twice a day. This gradually got better. It took about two months for this to get better. My back never bothers me at all. It felt numb for a while and for quite a while after I went back to work, I used to get sick to my stomach every time I would do any stooping, but right now I never felt better in my life. I have never had any of those ulcer pains any more."

These fragmentary quotations illustrate the hesitancy which one must exercise before assigning a "good" result to a patient simply because his ulcer symptoms have disappeared.

If one treats a man of forty, suffering from an unobstructing painful duodenal ulcer, by subtotal gastrectomy, he is deliberately turning his back on the possibility that an excellent result may be produced by a simple physiologic procedure which does not interrupt the continuity of the gastro-intestinal tract. The surgeon is also assuming the risk of a hospital mortality, which, while low is far from negligible. He may also encounter complications relative to function of the stoma, nutritional difficulties, anemia, "dumping" syndrome and other side-effects of gastrectomy which are every bit as bothersome to the patient as the side-effects of vagus resection.

In the last analysis, vagus resection must compete with subtotal gastrectomy as the operation of choice in intractable ulcer. As time goes by, we can hope that critical analyses of the side-effects and failures of subtotal gastrectomy will become available in increasing numbers.<sup>3</sup> The literature on subtotal gastrectomy has perforce often dealt with hospital mortality,<sup>4</sup> or the laboratory rationale of the procedure.<sup>5</sup> Unfortunately, neither of these considerations are particularly appropriate in comparing the operation with vagus resection. The hospital mortality of subtotal gastrectomy will probably always be higher than vagus resection, providing both operations are essayed by surgeons of comparable training. This condition arises simply from the fact that in vagus resection the gastro-intestinal tract is not entered or transected, and vagus resection is not applicable to those types of ulcer which produce much of the gastrectomy mortality rate such as acute massive hemorrhage or advanced cicatricial obstruction.

The low mortality of vagus resection cannot alone justify its performance. The operation must be able to show results which are as good as or better than subtotal gastrectomy in order to replace the latter. It is unlikely that in any large series of cases posterior gastro-enterostomy can be performed with or following vagotomy without somewhat increasing the hospital morbidity and mortality from the vagus resection.<sup>6</sup> If this is the case, one would again be led away from gastro-enterostomy as an adjunct to vagus resection.

Possibly vagus resection will finally come to occupy the role of a "clean-up" procedure to put to right the failures of other forms of surgery. This is a view with which the author is not in agreement. If vagus resection can stand on its own merits, it will have usefulness. If it has failures, those failures will most likely occur in patients who have had gastro-enterostomy, either with or without subtotal resection. Therefore, vagus resection used to "clean-up" the jejunal ulcers following other procedures, while of temporary benefit, may not be of lasting worth. The use of vagus resection as a secondary procedure will stand or fall wholly upon this consideration: is vagus resection a sound procedure for ulcer by itself, unaided and unhindered by previous or subsequent gastric surgery?<sup>7</sup>

Careful work in several clinics has now been going on for a period between three and four years.<sup>7-15</sup> The perspective of time will be needed to help us make a decision as to the final place of this operation. Its injudicious perform-

ance for gastric ulcer, the indiscriminate use of gastro-enterostomy with the procedure, hasty operative technique with inadequate section of the nerves, and operation on patients who are inadequately studied and inadequately followed, are all to be condemned as features which will prolong the difficult phase of evaluation of this operation. The statement has been made that "vagotomy is not an experiment that should be undertaken simultaneously in many quarters"<sup>16</sup> This statement is most assuredly a wise one. It is hoped that in those quarters where vagotomy is not being studied, the results of subtotal gastrectomy may be evaluated in the same critical fashion that the results of vagus resection have been studied, with an eye towards the symptomatic end-result, so that the comparison of subtotal gastrectomy with vagus resection may be facilitated.

#### SUMMARY

1 The results of vagus resection for ulcer carried out in 74 cases have been described.

2 Satisfactory results have been obtained in approximately 90 per cent of the cases.

3 A poor result may be due to difficulty with ulcer, but may also occur when the side-effects are of a massive and crippling type, the minor gastro-intestinal side-effects are not vitiated by the performance of gastro-enterostomy.

4 Good results have been obtained in patients who were intractable to all other forms of therapy including subtotal gastrectomy.

5 Vagus resection is an addition to the surgical armamentarium which may come to occupy a permanent and important place.

6 A reserved attitude must be maintained until the present groups of patients have been followed longer.

7 The routine performance of posterior gastro-enterostomy coincident with vagus resection may so confuse results that in the future one will not know whether to assign the end-result, whether good or bad, to the gastro-enterostomy or the vagus resection.

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A STUDY OF THE RESULTS, BOTH FAVORABLE AND UN-  
FAVORABLE, OF SECTION OF THE VAGUS NERVES  
IN THE TREATMENT OF PEPTIC ULCER\*

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DRAGSTEDT'S REPORT IN 1946 on the section, with favorable results, of the vagus nerves in 54 cases of peptic ulcer, and similar reports by Grimson,† Ruffin and co-authors<sup>4, 5, 13</sup> concerning 30 such operations at Duke University, and by Moore and his associates concerning 12 cases in which the operation was carried out at the Massachusetts General Hospital, led us to study the

TABLE I  
COMPARATIVE STATISTICS OF REPORTED VAGOTOMIES YEAR 1947

Reporter	Cases	Performed for ulcer, type					
		Duodenal		Gastrojejunal		Gastric	
		Number	Per cent	Number	Per cent	Number	Per cent
Dragstedt	170	147	87	15	8.8	8	4.7
Walters and associates	83	54	65	24	28	5	6
Walters (alone)	40	28	70	7	17	5	12
Grimson	57	32	56	9	15	4	7
Moore .	74	57	77	16	22	1	1

problem of section of the vagus nerves or, as we prefer to call the operation, "gastric neurectomy," from the anatomic, physiologic and chemical standpoints among 40 patients operated on by one of us (Walters) at the Mayo Clinic up to January 15, 1947 (Table I). Only brief reference will be made to a control series of 43 additional cases in which the operation was performed by other surgeons at the clinic, for the surgeons in question will individually report on their results in detail later.

HISTORICAL ASPECTS

Denervation of the stomach in the treatment of pain in peptic ulcer has been extensively investigated since Brodie's first report in 1814. Indeed, the operation has been performed in rabbits to assist in the experimental formation of gastric ulcers.

\* Read at the meeting of the American Surgical Association, Hot Springs, Virginia, March 25 to 27, 1947.

† In Grimson's most recent report on the results of the operation in 57 cases, he described disturbances in motility in 25. In six cases there was severe gastric retention which necessitated gastro-enterostomy. This gave an incidence of secondary gastro-enterostomy in one among each seven patients who had not had a previous drainage operation.

Reports in the literature are extensive and confusing. Time permits only the briefest reference to some of the most important clinical and experimental studies. One of the most interesting reports is that of Latarjet<sup>9</sup> in 1922. His studies are worthy of evaluation in view of the fact that he and Pauchet performed the operation on six patients who had gastric ulcers, after they had carried out extensive experimental studies on the effects of section of the vagus nerves of dogs.<sup>8</sup> In commenting on the results of the operation in six, Latarjet stated that all were relieved of their symptoms and that they had gained in weight and appetite. Gastro-enterostomy had been performed for all of them at the time of the denervation procedure, but one died later of carcinoma of the stomach.<sup>9</sup>

No additional reports by Latarjet or his associate, Pauchet, are found in the literature regarding later results of these operations.

McCrea, after confirming the experimental work of Latarjet, stated, however, that Lichtenbelt had found gastric ulcerations in 70 per cent of his dogs after complete section of all of the parasympathetic and sympathetic branches of the vagus nerves. In 1931 Beaver and Mann found that after performing the Mann-Williamson operation on dogs, ulcers formed in two of the three dogs of the series despite previous section of the vagus nerves. Recent studies by Grindlay and Bollman seem to confirm the results of earlier studies by Beaver and Mann. In addition, Grindlay and Bollman produced peptic ulcers by the administration of cinchophen. They found that ulcers developed whether or not the vagus nerves were sectioned, although the vagectomized dogs maintained a better nutritional state and lived longer, on the average, than did the control animals.

The preliminary studies of Saltzstein, Sandweross, Hammer and Hill, recently presented, would indicate that, after section of the vagus nerves in dogs on which the Mann-Williamson operation was performed, jejunal ulcers developed in four of nine animals who died within 41 days following operation. Six of the nine had marked jejunitis.

In 1929 Hartzell studied the effects on dogs of section of the vagus nerves. Although the immediate observations were similar to those noted among human beings, when Vanzant studied the dogs two-and-a-half years later she found that free hydrochloric acid had returned to the gastric secretion in all but one of the original group. Some of the dogs still had delayed emptying of the stomach, but two of the dogs had hypermotility, with a tendency toward diarrhea and emesis. Later studies revealed the gastric motility to be essentially normal.

#### ANATOMIC STUDIES

In studying the problem, we thought it essential to determine the anatomic distribution of the vagus nerves immediately above and below the diaphragm. Hence, dissections were carried out in our department of pathologic anatomy on 56 men, 44 women and 11 children during the course of postmortem examinations.

In 92 of the specimens from adult persons studied at necropsy a rather regular pattern was followed in the formation of discrete nerve trunks from the esophageal plexus. In eight cases it was impossible to isolate two distinct trunks at any point, since the branches were numerous and did not have a uniform pattern.

These anatomic studies indicate, therefore, that excluding the 11 cases in which the vagus nerves of children were dissected out, the vagus nerves can be located and successfully sectioned near the diaphragm in approximately 92 per cent of the cases, and possibly most, if not all, of the branches in the remaining 8 per cent of cases can be sectioned by either a transabdominal or a transthoracic approach.

#### GASTRIC NEURECTOMY WITHOUT OTHER GASTRIC OPERATIONS

It is our belief that the transabdominal approach is preferable to the transthoracic one because it permits exploration of the contents of the abdomen, examination of the ulcer, removal of the ulcer if this is thought to be advisable, and the performance of a gastric drainage operation, such as gastroenterostomy, or partial gastrectomy independent of, or coincident with section of the vagus nerves.

In only 14 of the 40 cases did we believe that the operation of section of the vagus nerves could be done without other surgical procedures on the stomach in order to prevent serious postoperative gastric retention. In 13 of the 14\* cases, results have been satisfactory as measured by relief of pain, reduction of acidity, and in general by reduction of gastric secretions. Ten of these operations were performed for duodenal ulcer, two were performed for gastric ulcer and two for gastrojejunal ulcer.

Of the ten patients who had duodenal ulcer, eight obtained a reduction of gastric acidity. In four of them the reduction was to an achlorhydria. For eight of the patients the Hollander insulin test was carried out. Results of this test in six cases showed a flat or decreasing curve of secretion of gastric acids. Results of the test in two cases showed a rise in the secretion of gastric acids.

There were disturbances of motility, with gastric retention, in four (40 per cent) of the cases. One patient required intermittent aspiration from the 4th to the 9th postoperative day, the remaining three were found to have considerable retained secretion and an atonic stomach as demonstrated roentgenologically.

In two patients who had small gastric ulcers achlorhydria developed after the operation. Results of insulin tests were negative. In one of the patients an atonic stomach developed which continued for at least eight weeks. Although this patient was relieved of pain after his operation, he complained of discom-

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\* The 14th patient, a man 39 years old, with a severe vascular disease, died suddenly in the anesthesia recovery room one hour after transabdominal gastric neurectomy. The patient's ulcer pain had been intractable to treatment. The risk of the operation was appreciated. At postmortem examination almost complete occlusion of the coronary arteries was found, caused by both arteriosclerotic and atheromatous changes in their walls.



fort and a sensation of fullness in his stomach after he had eaten a small amount of food at meal time. At the time of his re-examination at the clinic, eight weeks after operation, the stomach was so dilated and there was so much secretion that the roentgenologist was unable to determine whether or not the gastric ulcer had healed. Unfortunately, gastroscopic examination was not made in this case, but will be done at the next visit of the patient.

Since this is the most important group of cases, because of the difficulty of evaluation of the effect of section of the vagus nerves if an associated gastric operation is done, it has been thought advisable to select an additional group of patients who also underwent only section of the vagus nerves by our surgical colleagues at the clinic. Whereas in all our cases the operation was done transabdominally, in 14 of their cases it was done transthoracically and in five cases it was done transabdominally.

#### CONTROL SERIES VAGOTOMY ONLY

*Transthoracic*—In the group in which the approach was transthoracic, five patients were operated on for duodenal ulcers and nine were operated on for gastrojejunal ulcers. Two patients who had duodenal ulcers and one who had a gastrojejunal ulcer obtained no reduction of gastric acidity. Postoperative roentgenologic studies of two of the nine patients (22 per cent) who had had gastrojejunal ulcers continued to disclose jejunitis. For one of these two patients a state of achlorhydria had been obtained, but no reduction of acidity occurred in the patient who had the duodenal ulcer. This patient also had considerable gastric retention.

Four of the five patients with duodenal ulcer had delayed emptying of the stomach, in one of the four this delay was so prolonged (two months) that anterior gastro-enterostomy was performed. The pylorus was found to be open, and the scar of the ulcer was present.\* In spite of this, the patient continued to have a large degree of gastric retention for more than 30 days. Another patient with duodenal ulcer continued to have ulcer pain and nocturnal pain, requiring food and alkalis for relief. Two patients had troublesome diarrhea, one had a return of symptoms of ulcer and the other had nausea and vomiting in addition.

*Transabdominal*—Two patients with duodenal ulcers and three with gastrojejunal ulcers underwent transabdominal gastric neurectomy. Only one of these patients obtained a good result, with complete relief of symptoms. One of the patients with a duodenal ulcer had symptoms of bloating, belching and vomiting four months postoperatively, and although he had no ulcer pain a roentgenogram disclosed a persistent duodenal ulcer.

One patient died after a convulsion on the 4th postoperative day. Unfortunately, consent for postmortem examination could not be obtained in this

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\* Since gastric neurectomy had been done transthoracically, the gross pathology of the duodenal ulcer could not be compared with its appearance at the time of gastro-enterostomy.

case This patient had also undergone cholecystectomy and appendectomy at the time of section of the vagus nerves

One of the patients with a gastrojejunal ulcer had persisting symptoms of ulcer Disturbances of gastric motility required aspiration for one month after operation The roentgenogram showed a poorly functioning gastroenteric anastomosis, with distortion of the jejunum, and the presence of a gastrojejunal ulcer could not be ruled out

#### GASTRIC NEURECTOMY WITH GASTRIC OPERATIONS

Time does not permit a detailed discussion of studies of patients for whom gastric neurectomy and operations on the stomach were carried out simultaneously or later because of failure of the ulcer to heal or because of recurrence of the ulcer or because of persisting gastric retention A detailed report of 26 cases will be made elsewhere

*Duodenal ulcer* —Suffice it to say at this time that among the 15 patients with duodenal ulcer on whom one of us (Walters) operated, performing gastro-enterostomy in addition to resection of the vagus nerves, a reduction of gastric acidity occurred in 11 (73 per cent), and in seven of these 11 (56 per cent) it reached the state of achlorhydria Troublesome disturbance of gastric motility developed in four (26 per cent) In one patient with a large obstructing duodenal ulcer, such a marked degree of abdominal distention developed from the 5th to the 7th day that an intestinal obstruction was thought likely Abdominal exploration revealed that the entire gastro-intestinal tract was filled with fluid and gas, and that 800 cc of sterile straw-colored fluid was present in the abdominal cavity The gastro-intestinal motility returned to within normal limits in a few days after continuous aspiration of the gastro-intestinal secretions by means of an indwelling gastric suction tube

Another patient had intermittent gastric retention daily, in which the fluid retained sometimes reached a maximum of 2,000 cc, with gradual reduction in the amount until the 14th postoperative day Six months later he reported by letter that the symptoms of ulcer had returned, and that vomiting had occurred

Another patient reported by letter three months postoperatively that he had considerable flatulence and diarrhea which were not relieved by the usual measures, such as the taking of paregoric

*Gastric ulcer* —Three patients underwent excision of ulcer in association with gastric neurectomy One patient was a man 67 years old for whom one of us (Walters) had performed removal of a gastrojejunal ulcer and a closure of his gastric and jejunal openings on June 14, 1946 He had a large gastric ulcer on the posterior wall of the stomach, the ulcer had perforated to the pancreas just below the esophagus To have removed it would have necessitated a very high partial gastrectomy, and it was thought that the situation was one which should be suitable for transthoracic section of the vagus nerves Six and a half weeks of medical treatment was administered after removal of the

gastrojejunal ulcer, but without benefit. Transthoracic section of the vagus nerves was carried out by Doctor Clagett and one of us (Walters) on June 29, 1946. In addition, the gastric ulcer was excised to exclude the possibility of malignancy. Although the immediate results of the operation seemed good—a state of achlorhydria was obtained as was also a negative result of the Hollander insulin test—within a period of a few weeks the patient began to complain again of abdominal pain. A roentgenogram at this time showed a recurrent large gastric ulcer in the same position as that of the ulcer previously excised. Concurrently, anemia appeared and free hydrochloric acid again returned to the stomach. The result of an insulin test was again negative, but high acid values for histamine stimulation were obtained. When resection of the stomach was performed, January 13, 1947, including removal of the large gastric ulcer (3.5 cm. in diameter), by our colleague, Doctor Waugh, the ulcer was reported as benign. Although the patient is out of the hospital, he reports that he is no better than he was before partial gastrectomy.

There was a second case in which a large gastric ulcer situated on the posterior wall was excised. The patient complained of frequent belching of foul gas four months after the operation. Roentgenologic examination showed a dilated stomach with so much secretion at the end of a five-hour period that the roentgenologist was unable to determine whether or not gastric ulceration had returned. Gastroscopic examination revealed no recurrence of the gastric ulcer. In this case, associated with the dilatation of the stomach, was hypomotility of the small intestine, with seeming spasm of the pylorus.

*Gastrojejunal ulcer*.—For one of the five patients operated on for gastrojejunal ulcers, re-resection of the stomach was performed in order to remove a large perforating anastomotic ulcer with its base on the colon. Removal of the gastrojejunal ulcers and closure of the openings of the stomach and jejunum were performed in the other cases, in two of which it seemed advisable because of the obstruction of the duodenum by the scar of the previous duodenal ulcer.

Among the patients who had gastrojejunal ulcers, immediate results of the operation have been very satisfactory.

#### CONTROL SERIES VAGOTOMY ASSOCIATED WITH OTHER OPERATIONS

In the control series of 24 patients who underwent gastric neurectomy and additional gastric operations performed by our colleagues, 19 patients were operated on for duodenal ulcer and five for gastrojejunal ulcer. Most important in the group was a patient with duodenal ulcer who, after section of the vagus nerves and gastro-enterostomy, died on the 14th day. Although his post-operative course was characterized by marked gastric retention and hypoproteinemia which was difficult to control, the presence of the perforated ulcer and subdiaphragmatic abscess was not recognized until demonstrated at post-mortem examination.

Resection of the stomach was performed for one patient who had a bleeding gastrojejunal ulcer. This patient had had transthoracic section of the

vagus nerves performed elsewhere six and a half months previously, without benefit

Eighty per cent of the patients obtained marked reductions of gastric acidity, 36 per cent to an achlorhydric degree. Temporary disturbances of motility were present in five or 31 per cent of the cases. As in our series, the relief of symptoms was no different than it would have been had associated gastric neurectomy not been carried out.

#### SUMMARY

Our studies on section of the vagus nerves indicate that the results are inconstant, variable, and in most cases unpredictable. The relief of pain obtained is probably brought about by release of gastrosplasm and reduction of gastric acidity as a result of the interruption of cephalic stimulation and as a result of other factors not now understood. The expense of this is dilatation of the stomach with frequent troublesome retention of gastric secretion and, in some cases, food remnants. Moreover, that relief of pain is not the result of healing of the ulcer must be considered, since in one of our cases an unsuspected acute perforation of duodenal ulcer developed. A similar case has been reported by Weeks and his associates.

Reduction in gastric acidity, although it has occurred in most cases, is inconstant in others, and disturbances of motility of the stomach and small intestine are of frequent occurrence after operation. In some cases such disturbances are temporary and in others they are prolonged, persistent and troublesome to the patient. In such cases, patients have complained of frequent belching of foul-smelling gas, a sensation of fullness and bloating after meals and, in a few cases, nausea and diarrhea.

In at least one clear-cut case the ulcer has been known to have recurred, and in the others the ulcers have failed to heal and reoperation has been necessary to remove the ulcers or to provide drainage of the stomach because of the troublesome gastric retention.

There have been three deaths in the hospital in the 83 cases. Although two of these could be attributed directly to cardiovascular accidents, one patient died of an unsuspected perforated duodenal ulcer with a subdiaphragmatic abscess. Gastro-enterostomy had been done in association with gastric neurectomy. Another patient died from coronary occlusion at home four months after closure of a gastrojejunal fistula.

In evaluation of the results of the operation, it must be proved that an ulcer is present and that the vagus nerves have been completely sectioned. It is our opinion that the best approach, in most cases in which gastric neurectomy is contemplated, is by means of a transabdominal incision, for such an approach allows both examination of the ulcer and exploration of the gastrointestinal tract and performance of such procedures as might seem necessary to supplement the gastric neurectomy. The greatest field of usefulness for gastric neurectomy seems to be in the treatment of ulcers after partial gastrectomy and in certain cases of nonobstructive duodenal ulcers in which the

cephalic phase of gastric secretion is marked and pain is intractable. If the operation is used in the treatment of gastrojejunal ulceration after gastroenterostomy the possibility of obstruction at the stoma and at the site of the healed or reactivated duodenal ulcer must be considered.

In view of the inherent ability of the gastro-intestinal tract of human beings, like that of the gastro-intestinal tract of animals in the experimental laboratory, to regain through anatomic and compensatory mechanisms its function after operative procedures which disturb neuromuscular continuity, and since restoration of gastric acidity and gastric motility has occurred within a two-year period in dogs in which gastric neurectomy has been performed, the possibility of such a return in human beings must be kept in mind constantly.

For the time being, the operation of gastric neurectomy must be considered to be in the investigative stage and the effects of the operation carefully studied.

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# SECTION OF THE VAGUS NERVES TO THE STOMACH IN THE TREATMENT OF PEPTIC ULCER\*†

Complications and End Results After Four Years

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and by invitation

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DURING THE PAST FOUR YEARS, division or resection of the vagus nerves to the stomach as a method of treatment has been employed in the Department of Surgery of the University of Chicago on 212 patients with various types of peptic ulcer. One patient died of aspiration pneumonia, making an operative mortality of something less than one-half per cent. Although a careful watch was made, no gross evidence of any serious disturbance that could be ascribed to a vagus reflex was encountered. The theoretical background for employing this procedure in the treatment of peptic ulcer has been presented in previous publications from this clinic<sup>1</sup>. It is the purpose of the present communication to describe the complications and end results of vagus section for peptic ulcer in 160 patients who were operated on by us during the four years from January 18, 1943, to January 1, 1947. In these 160 patients, the vagus section was complete in 142 cases as evidenced by a reduction in the night secretion of gastric juice, a decrease of over 60 per cent in the total hydrochloric acid output from the stomach, and a negative secretory response to insulin hypoglycemia. Persistence or recurrence of ulcer symptoms has not been seen in any of these patients, and at the present time, all of them are free of ulcer distress without medication or any type of dietary restriction. In most cases, there is also satisfactory objective evidence that the ulcers have healed. In the 18 patients where physiologic tests have indicated that the vagus section was not complete, 13 have remained free of ulcer symptoms without medication or dietary restriction. In the remaining five, persistence or recurrence of ulcer symptoms in varying degree have been observed. In two of the patients, the symptoms were sufficiently severe so that our proposal for a reoperation was accepted. One of these patients had been operated upon by the transthoracic and one by the transabdominal approach. Reoperation in each case was done by the transabdominal method. In both instances, a remaining vagus fiber was found and sectioned. The results are summarized in Tables I and II. In three of the patients where recurrence of symptoms has been observed, these have been so mild that no treatment has been desired. The 13 patients in whom we

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have reason to believe that the vagotomy was incomplete, but who at present are free of ulcer symptoms without medication or dietary restriction, are being watched with great interest. It seems probable on the basis of present information that to be effective, the vagus section must be complete, and that recurrence or persistence of ulcer symptoms may occur if even a small vagus fiber to the stomach has been overlooked. This observation is of interest when correlated with the effect of vagus section on gastric secretion. Section of one of the vagus nerves in dogs has no effect on the volume, acidity, or total output of acid in the gastric secretion. In man, apparently the persistence of a small vagus fiber after section of two of the larger vagal trunks permits the continued excessive night secretion characteristic of the ulcer patient. The remaining vagus fiber appears to be able to activate the entire glandular apparatus, acting presumably through the submucous plexus of Meissner.

TABLE I

Patient J S	Male	Age 57			
Five-year history of duodenal ulcer with two massive hemorrhages					
September 10 1945	TRANSTHORACIC VAGOTOMY				
Night Secretion	Volume	Free Acid	HCl Output	Insulin Test	
Preoperative	1 375 cc	24	34 m e	Pos	
Postoperative	1 065 cc	36	38 m e	Neg	
Patient entirely well in the interim on full diet and without medication					
November 23 1946	Silent massive hemorrhage				
December 12 1946	TRANSABDOMINAL VAGOTOMY				
Night Secretion	Volume	Free Acid	HCl Output	Insulin Test	
Preoperative	1 200 cc	62	74 m e	Pos	
Postoperative	640 cc	23	15 m e	Neg.	

TABLE II

Patient L H	Male	Age 42			
Six year history of duodenal ulcer					
October 10 1946	TRANSABDOMINAL VAGOTOMY				
Night Secretion	Volume	Free Acid	HCl Output	Insulin Test	
Preoperative	970 cc	13	13 m e	Pos	
Postoperative	858 cc	29	25 m e	Pos	
Relief of symptoms for one month post operatively			Then recurrence of all previous symptoms		
January 5 1947	TRANSABDOMINAL VAGOTOMY				
Night Secretion	Volume	Free Acid	HCl Output	Insulin Test	
Preoperative	870 cc	18	16 m e	Pos	
Postoperative	410 cc	0	0	Neg	

Where the vagotomy has been complete, there is to date no evidence of regeneration of the secretory fibers in the vagus nerves. Re-examination of these patients has been made at intervals by measuring the night secretion of gastric juice, the total hydrochloric acid output, and the secretory response to insulin hypoglycemia and the sham meal. Since an interval of three and four years has elapsed in a number of these patients, it seems quite probable that the nervous phase of gastric secretion has been permanently abolished. The evidence obtained from the experimental laboratory on the pathogenesis of peptic ulcer suggests that the ulcers will not recur unless the previous excessive secretion returns. The outlook is accordingly much more favorable than the present limited period of clinical observation would justify.

POSTOPERATIVE MANAGEMENT

The complications following gastric vagotomy for peptic ulcer have been for the most part transitory and inconsequential. In 61 patients, the vagus section was performed by a transthoracic operation. One of these patients developed an aspiration pneumonia which proved fatal. This was the only death in the series and occurred early in our experience. There have been no deaths in the last 150 vagotomies. A pleural effusion requiring aspiration was encountered in six patients. In no case did this effusion become infected. Inter-costal pain in the region of the incision proved troublesome in ten patients, and in these, persisted for a period of two to four weeks.

*Gastric Retention* It is probable that a delay in the emptying of the stomach occurs in all patients following section of the vagus nerves. This delay produced transitory symptoms in 19 of the 61 patients in whom a transthoracic vagotomy was performed. In four the gastric retention was severe enough to necessitate a gastroenterostomy within two or three months following the vagus section. In each of these cases, cicatricial obstruction at the pylorus was found. The necessity for a second operation in these four patients prompted us two years ago to explore the possibility of securing a complete vagus section by a transabdominal approach. The remarkable elasticity of the esophagus, which was appreciated in the transthoracic operation, suggested that it ought to be possible to pull the esophagus downward into the abdomen sufficiently to permit careful exploration of its lower three or four inches. We are now convinced that it is just as possible to secure a complete section of the vagus nerves to the stomach by a transabdominal operation as can be secured by the transthoracic approach. The method that we presently employ is best described in a series of diagrams and drawings (Figs 1-4). We prefer the transabdominal operation at the present time because it is possible to deal with cicatricial obstruction at the pylorus at the same procedure. Of the patients who were operated upon by the abdominal route to January, 1947, in 64 cases, the abdominal vagotomy was accompanied by a posterior gastroenterostomy, while in 35 patients, a vagus section alone was performed. In the first patients, the gastroenterostomy was added as a routine in all patients with duodenal ulcer, but for the past year, it has been employed only when pyloric obstruction has been indicated either by clinical symptoms or fluoroscopic findings. At the present time, posterior gastroenterostomy is being performed in approximately one-third of the patients for whom a transabdominal vagus section is done for duodenal ulcer. In the 35 patients with duodenal ulcer in whom vagus section alone was performed, 19 patients displayed transitory symptoms of gastric retention. Two subsequently required a gastro-enterostomy because of cicatricial obstruction at the pylorus. Of the 64 patients in whom a gastroenterostomy was performed at the time of the abdominal vagotomy, eight patients showed transitory symptoms of gastric retention but have subsequently remained well.

*Stomach Motility and Tonus* It is probable that more difficulty would have been encountered from the decreased tonus and motility of the stomach



produced by vagus section had its possibility not been anticipated and measures taken to prevent it. The stomach like the heart and the amphibian lung possesses a local automatism which is largely due to its relation to Auerbach's plexus. This makes it possible for the stomach to display its normal motility after all extrinsic nerves have been severed, or even after the stomach has been removed from the body. Under normal conditions, however, its activity is under the influence of two sets of extrinsic nerves. In general, the vagus nerves exert an inhibitory influence over the motor activity of the cardia, an

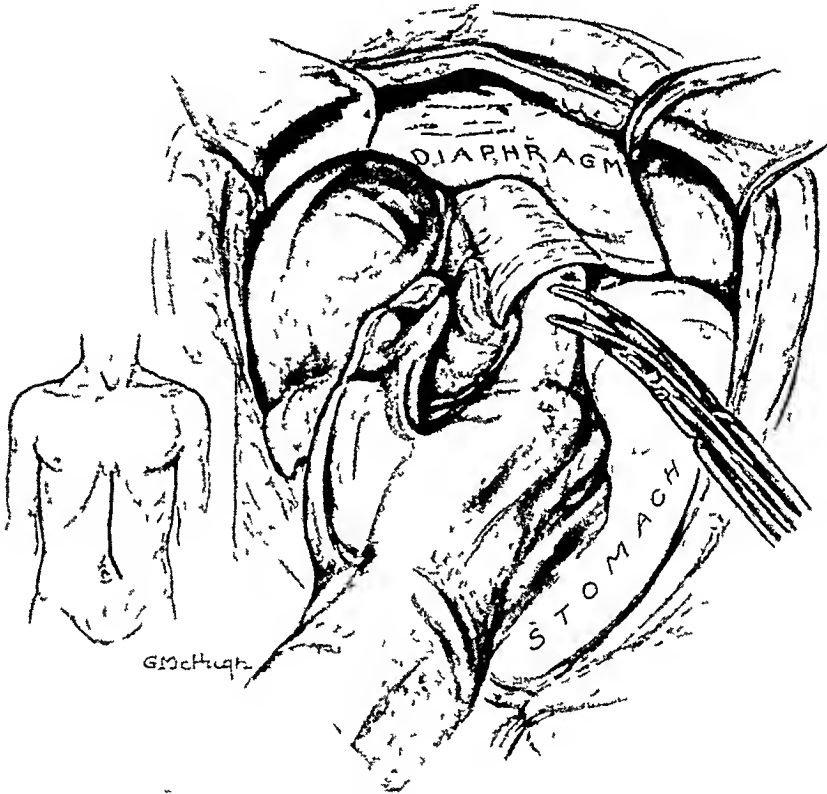


FIG 1.—The abdomen is opened through a high left paramedian incision. The triangular ligament to the liver is divided.

augmenter influence on the body of the stomach, and an inhibitory influence on the pylorus. In general, the effect of the sympathetic is antagonistic to that of the vagus. A sudden removal of the tonic effect of the vagus nerves leaves the inhibitory influence of the sympathetics unopposed, and the end result is to cause a marked inhibition in the tonus and motility of the stomach. This makes the stomach very susceptible to the dilating effect of swallowed air or accumulated secretion, and if care is not taken, an acute dilatation can quite readily be produced. After a period of time which varies in different patients, a readjustment of the peripheral motor mechanism occurs, and the motility of the stomach returns toward its normal state. It is likely that it never regains the hypertonus and hypermotility so commonly found in ulcer patients. It has been

our practice to guard against distention of the stomach during the immediate postoperative period by maintaining gastric decompression by means of a Levine tube and the Wangenstein suction apparatus for a period of five days following the vagus section. This is perhaps the most important single item in postoperative care. After the five-day period, the patient is given small amounts of water, and at the end of 12 hours, the stomach is aspirated to

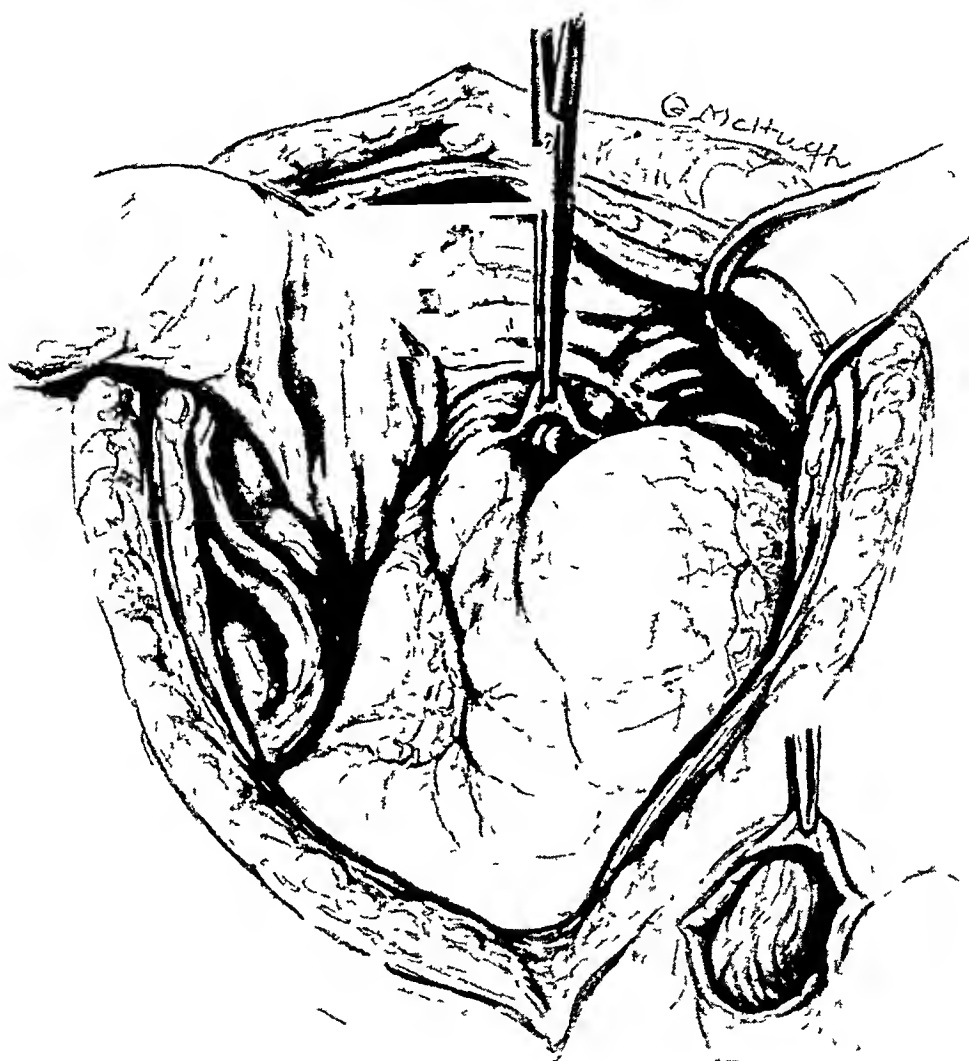


FIG 2—The left lobe of the liver is retracted to the right, and the peritoneum over the esophagus at the margin of the diaphragm is divided and the hiatus opened

determine if retention has occurred. If the stomach is not emptied, decompression is instituted and maintained for another 24 to 48 hours. Only when the stomach empties itself satisfactorily of liquid content is the patient permitted to ingest solid food. The amount ingested at any one feeding is limited, and the patient is cautioned not to overload the stomach during the first two or three months after the operation. In several patients, we have felt that the return of function or readjustment of the peripheral motor mechanism of the stomach was facilitated by giving the patient ten mg of urecholine from an hour to 30 minutes before the ingestion of food. This drug produces a long

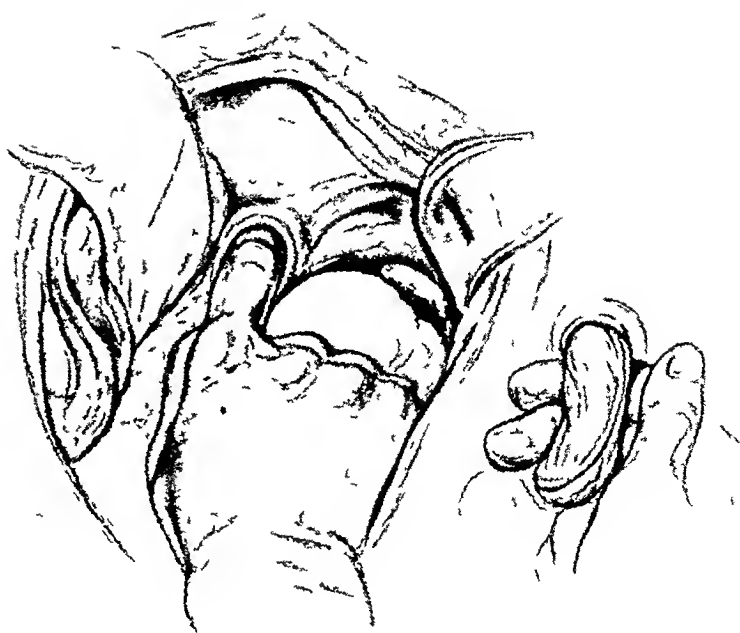


FIG 3—The finger is introduced over the esophagus into the mediastinum, the esophagus mobilized by careful finger dissection and pulled downward into the abdomen for a distance of 2 to 3 inches

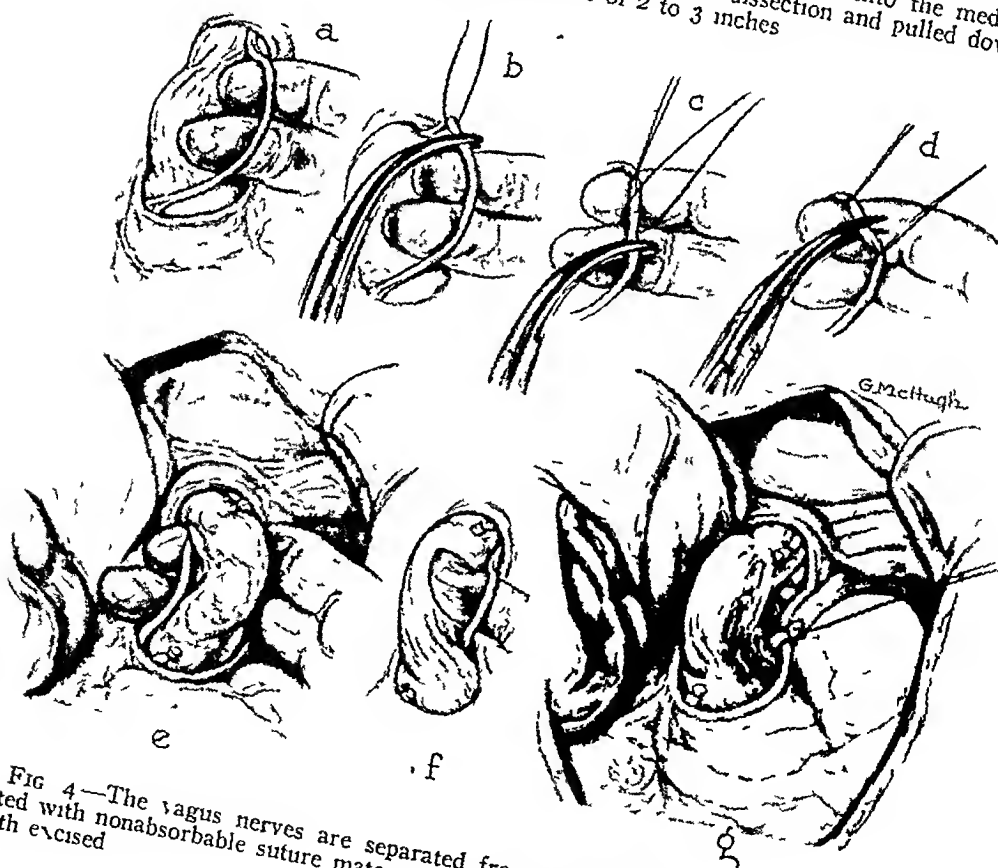


FIG 4—The vagus nerves are separated from the esophagus by finger dissection, ligated with nonabsorbable suture material, divided, and a segment 4 to 6 centimeters in length excised

continued increase in the motility of the stomach probably through stimulation of the peripheral neuromotor mechanism. That this readjustment in gastric motility can be confidently expected is indicated by the fact that none of the patients who were operated upon by us during the first three years are at present experiencing any difficulty on this score.

*Alteration in the bowel habit* was encountered in 25 of the 61 patients who underwent transthoracic section of the vagus nerves. In 18 of these patients, the effect was slight and transitory and usually elicited only by question. In seven patients, however, there was a moderately severe diarrhea, in some cases lasting from two to five weeks after the operation. This diarrhea was usually episodic in character with frequent long intervals of freedom between attacks. There appeared to be an association between the diarrhea and symptoms of gastric retention. The cause of this diarrhea has not been fully determined. Since division of the vagus nerves removes the augmented influence of this system from the tonus and motility of the small intestine and the proximal half of the colon, a change in the bowel habit in the direction of stasis or constipation was anticipated. To our surprise, this has not been encountered in a single patient. It is doubtful if the diarrhea can be ascribed to an increased motility of the small intestine and colon due to removal of vagal influences since it is most likely that this occurs in every patient who undergoes a partial or subtotal gastric resection. A consideration of the anatomy of the vagus nerves to the stomach makes it seem very probable that the usual type of gastric resection removes the vagus innervation from all structures below the stump of stomach that remains. The gastric contents following complete vagotomy usually contain no free acid during the digestive period when food is present in the stomach. The removal of the antiseptic action of the free acid of the gastric juice probably makes these patients more susceptible to diarrheas of bacterial origin. The situation here may be similar to that obtaining in patients with anacidity from other causes such as pernicious anemia. Retention in the stomach in combination with this anacidity makes fermentation possible and the consequent elaboration of various irritant organic acids. In the 64 patients with duodenal ulcer in which an abdominal vagotomy plus gastroenterostomy was performed, diarrhea, slight and transitory in character, was encountered in only four patients. Since gastric retention was less evident in these patients than in those with vagotomy alone, it seems likely that this factor is of some significance in the cause of the diarrhea. The diarrhea has usually subsided promptly when gastric decompression has been resumed. Spontaneous recovery from the diarrhea has usually accompanied readjustment of the motor activity of the vagotomized stomach and intestines, and none of the early patients are experiencing any difficulty on this account.

In the dog, section of the vagus nerves high in the chest or in the cervical region almost invariably produces a high grade and long continued spasm of the cardia and of the pylorus. For this reason, it is of great interest that we have not encountered spasm of the cardia in a single patient following vagus section. This is probably due to the fact that the vagi are usually

divided a short distance above the diaphragm. It is quite possible that damage to the vagus nerves higher up might produce spasm of the cardia in man as it does in the lower animals. In two patients, edema of the lower esophagus, probably due to the trauma of the operation, caused temporary dysphagia. The passage of the esophagoscope promptly gave relief without recurrence.

In summarizing our experiences with complete section of the vagus nerves to the stomach in the treatment of peptic ulcer, it appears clear that this operation, as we have described it, abolishes permanently the nervous phase of gastric secretion, and likewise removes the augmenting influence of the vagus nerves on the tonus and motility of the stomach and small intestines. It is probable that both the effect on gastric secretion and on motility exert a favorable effect on the healing of peptic ulcers. It is probable that the depressing effect on the secretion of gastric juice is the more important factor in bringing about the healing of the lesion. The decrease in the tonus and motility of the stomach probably also exerts a beneficial influence in the same direction, and undoubtedly contributes much to the relief of the distress which these patients experience. Both of these effects are likewise mainly responsible for the undesirable sequelae and complications of the operation. We should like to emphasize, however, that these complications in our experience have been self-limited, and for the most part inconsequential as compared to the complications that have been described following subtotal gastrectomy for peptic ulcer.

One of the most conspicuous effects of section of the vagus nerves to the stomach in patients with peptic ulcer is the immediate, complete, and apparently permanent relief of the ulcer distress that is produced. We have frequently called attention to this phenomenon which is so marked that in our early experience led us to speculate on the possibility that the stomach had been rendered anesthetic by the operation. Subsequent experience, however, has convinced us that this is not the case. In the operations that have been performed by the transabdominal route, the anesthetic has been for the most part continuous spinal. Under these conditions, mobilization, pinching, ligating, and dividing the vagus nerves have not produced any sensation. A more crucial experiment, however, has been performed on five patients who had very severe ulcer pain when they came to the hospital. In these patients, it was found that aspiration of the gastric content usually provided immediate relief. The reintroduction in the stomach of 200 cc. of 5 per cent hydrochloric acid solution caused an almost immediate reappearance of typical ulcer pain and distress. Following the operation, all of these patients were immediately and completely relieved. Usually on the third day following the operation, without the knowledge of the patient, the Wangenstein suction apparatus was discontinued, and 200 cc. of 5 per cent hydrochloric acid solution was instilled into the stomach. Within a period of one to nine minutes, the former typical ulcer distress reappeared in all of its former severity. While this experiment does not necessarily prove that the ulcer pain and distress is due directly to the free hydrochloric acid, since the motility of the stomach was not simultaneously



Fig 5—X-ray film showing a large gastrojejunal ulcer crater following antral exclusion and subtotal gastric resection



Fig 6—X-ray film showing definite decrease in gastrojejunal ulcer crater 25 days after transthoracic vagotomy



FIG 8—X-ray film showing absence of gastrojejunal ulcer crater 21 months after transthoracic vagotomy and also retrograde filling of the duodenum and antrum of the stomach



FIG 7—X-ray film showing complete disappearance of gastrojejunal ulcer crater 47 days after transthoracic vagotomy

studied, it does indicate that the stomach has not been rendered anesthetic by the operation

The beneficial effect of vagus section in the healing of peptic ulcer is especially well illustrated in 14 of our patients in whom this operation was done for recurrent gastrojejunal ulcer following either gastroenterostomy or subtotal gastric resection. A detailed report of these findings has been published elsewhere. We should like to refer here to an additional patient with a gastrojejunal ulcer who presents some features that are of special interest. The patient, a male age 36, was first seen on August 29, 1938. For the previous two months, he had been complaining of typical ulcer distress, and x-ray examination revealed a duodenal ulcer with a crater. Symptoms were controlled for a time on medical management but recurred in severe form in 1943, and surgery was requested. At operation, a large, chronic, duodenal ulcer penetrating into the pancreas was found. Because of the extensive involvement, a Finsterlein-Devine type of exclusion operation was performed with subtotal gastric resection. Six months after the operation, a recurrence of symptoms developed, and a gastrojejunal ulcer was demonstrated at x-ray. X-ray therapy to the stomach was then given with relief of symptoms, and there was apparent disappearance of the ulcer crater. The symptoms recurred in six months, and the pain became more severe. X-ray examination again revealed an ulcer crater (Fig 5). On March 23, 1945, a transthoracic supra-diaphragmatic section of the vagus nerves was performed. Recovery was uneventful, and the patient was entirely relieved of ulcer distress. X-ray examination on April 16, 1945, revealed definite decrease in the size of the ulcer crater (Fig 6), and on May 9, 1945, complete disappearance of the crater (Fig 7). He remained well, resumed his former occupation, and was able to eat an entirely unrestricted diet without any type of medication. Fluoroscopic examination of the stomach was made in December, 1946, and the findings proved to be most interesting (Fig 8). The film shows no trace of an ulcer crater, and the stomach and jejunum are well outlined with barium. Of great interest is the demonstration of a retrograde passage of the barium through the duodenum, the pylorus, and into the antrum of the stomach, which was left behind at the time of the operation. The increased incidence of gastrojejunal ulcer following gastric resection in which the antral mucosa is left unremoved has been well recognized. The explanation offered for the high incidence of jejunal ulcers in these cases is that this mucosa makes possible the continued excessive secretion of gastric juice, presumably through the elaboration of gastrin as called for in the hypothesis of Edkins. The work of Edkins, however, indicated that gastrin is liberated from the antral mucosa only on contact with food. Here is visual evidence that a retrograde passage of the gastric content through the duodenum, through the pylorus, and into the antrum, can occur, which fulfill the requirements for the liberation of gastrin and its stimulating action on the gastric glands. It is significant, therefore, that in this patient a large jejunal ulcer healed following complete



vagus section, even though that part of the humoral mechanism for gastric secretion controlled by the antral mucosa was still present

### SUMMARY AND CONCLUSIONS

During the period from January 18, 1943, to March 1, 1947, division or resection of the vagus nerves to the stomach as a method of treatment has been employed in the University of Chicago Clinics in 212 patients with various types of peptic ulcer. One patient died of aspiration bronchopneumonia, and there have been no deaths in the last 150 vagotomies performed. Adverse reflex effects that might be ascribed to stimulation of the vagus nerves have not been seen. The clinical results of the operation have been excellent and have led us to the impression that a benign peptic ulcer may be regularly expected to heal if all the vagus fibers to the stomach are divided. This is best accomplished by exposure of these nerves along the lower esophagus by either a transabdominal or a transpleural approach. The transabdominal operation has the significant advantage that it makes possible inspection and palpation of the lesion and the performance of a gastroenterostomy should cicatricial obstruction at the pylorus be present. Gastric vagotomy abolishes the nervous phase of gastrin secretion and decreases very markedly the total amount of gastric juice produced. These effects appear to be permanent. Evidence of regeneration of the secretory fibers in the vagus nerves has not been observed even in the patients operated upon four years ago. These findings suggest that regeneration of the divided vagus fibers will not prove to be a troublesome feature of this type of operation. Complications and undesirable sequelae that have been encountered are intercostal pain or neuralgia, pleural effusion, pulmonary atelectasis, delayed emptying of the stomach, and diarrhea. For the most part, these complications have been mild and self-limited. Careful attention to post-operative care reduces the incidence and severity of most of them. Persistence of ulcer symptoms has been observed in five patients, and in these, physiologic tests have indicated that not all the vagus fibers were divided. In two of these patients, a second operation was performed, and a residual vagus fiber was discovered and divided.

These findings suggest that to be effective in abolishing the nervous phase of gastric secretion and causing the healing of benign peptic ulcers, removal of the vagus innervation of the stomach must be complete. It is probable that the poor results secured by the early workers in this field are due to the fact that attempts were made to section the vagus nerves in operations directed at the stomach instead of the esophagus and thus were in all probability incomplete. The necessity of repeated physiologic tests to determine residual vagal innervation of the gastric glands is clear and should be emphasized.

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DISCUSSION—DR KEITH S GRIMSON, Durham, N C I wish to thank Dr Walters and Dr Firor for arranging the privilege of the floor, and to congratulate Dr Dragstedt, Dr Moore, Dr Walters and Dr Griswold on their excellent studies There can be little doubt now that Dr Dragstedt's reintroduction of vagotomy has profoundly influenced surgical management of ulcer This is best evidenced by the 500 cases reported this afternoon including our 77, and by the continuing use of vagotomy by each author even though few cases have been followed for more than two years

Since vagotomy is in a stage of evaluation, I should like to express agreement with certain observations presented First, with very few exceptions healing or quiescence of ulcer occurred Failure in two of our patients necessitated secondary subtotal gastric resection Second, changes of acidity and motility have been variable, but usually acidity of fasting gastric content and response to histamine or insulin hypoglycemia have been reduced and emptying of the stomach delayed There has been some evidence that some but not all of these variations may be caused by incomplete vagotomy Excellent clinical results have occurred, however, in patients with a positive insulin test Since changes of secretion and motility usually persisted in patients studied for two or three years, regeneration is not likely to be a limiting factor

Unfortunately we have had more trouble with complications than most Greatest has been the necessity for performing seven secondary gastroenterostomies, or one among each seven patients who did not already have enterostomy Gastric retention six hours after taking barium has been greater than 30 per cent in all patients without gastroenterostomy and often 50 to 90 per cent It is our belief that physiologic obstruction of the outlet of the stomach occurred and was a more important cause of retention than scarring from ulcer Resting intragastric pressure or tone, according to our observations, increased slightly after vagotomy Gastric retention was relieved by gastroenterostomy or occasionally by urecholine or doryl Diarrhea occurred in some patients Although complications have been serious at times, most patients are relieved of symptoms of ulcer, satisfied and able to work Only a few have not gained weight At the present time we are employing subdiaphragmatic vagotomy with pyloroplasty, exclusion or gastrojejunostomy for duodenal ulcer, and reserving transthoracic vagotomy alone for stomach ulcer

DR RALPH COLP, New York I have had the privilege of previously reading Dr Walters' interesting communication From our limited experience I agree that the results following the severance of the vagus nerves to the stomach in the treatment of peptic ulcer are "inconsistent, variable and in most cases unpredictable" I shall not discuss the effects of vagotomy on acid secretion I shall confine my comments mainly to the post-operative motor difficulties which apparently bear little relationship to the completeness or incompleteness of the division of the vagi as revealed by the insulin test

I should like to present a series of 20 cases of chronic duodenal ulcer without obstruction At that time, we performed supradiaphragmatic vagotomy All cases but one follow-

ing operation were immediately relieved of pain. This patient was explored two months later. In spite of a negative insulin response, an active posterior wall duodenal ulcer was found and a subtotal gastrectomy was performed. Eight patients have remained well from three to eight months. Eleven of these patients following supradiaphragmatic vagotomy complained of epigastric fullness, gastric oppression, foul eructations and vomiting due to gastric dilatation with retention. In seven, symptoms eventually disappeared in from one to seven months, but four failed to respond to medical treatment in spite of repeated hospitalizations. These patients were so miserable that they requested surgical therapy in from six to eight months following supradiaphragmatic vagotomy. In these cases (Table II) surgical exploration revealed that the ulcer had healed, that the pylorus was patent in all, but in three the stomach was markedly dilated. In the latter instance a subtotal gastrectomy was performed. The immediate postoperative course was uneventful and at no time since have there been any symptoms which could be ascribed to gastric atony. In one patient in whom exploration disclosed a slightly dilated stomach, a dilated duodenum and colon, nothing was done. He still remains miserable.

Twenty cases is admittedly a small series, but the fact that five of these patients required another surgical exploration, one for persistent pain and four for intractable motor disturbances, has convinced us that severance of the vagus nerves as a sole procedure should not be offered to patients with chronic duodenal ulcer without obstruction as a reliable therapeutic measure. We therefore have discontinued it for the present.

In our first 33 cases the vagi were divided transthoracically (Table I). In our last 44 patients we have used the infra-diaphragmatic approach (Table III). The exposure and division of the vagi beneath the diaphragm is perfectly satisfactory. This method has the distinct advantage in that it permits a thorough abdominal exploration and offers an opportunity for studying the gross pathology of the local lesion. We have performed an infradiaphragmatic vagotomy with complementary gastroenterostomy in 15 patients whom we did not consider to be suitable risks for subtotal gastrectomy. Aside from one aged patient who died from a peritonitis, incident to secondary jejunostomy for alimentation due to gastric atony, the remainder have not suffered from any prolonged postoperative disturbances. From past experiences it is known that symptoms of a duodenal ulcer *per se* are invariably relieved by gastroenterostomy, and that the ulcer heals. The unfortunate disadvantage of this simple operation is the high incidence of gastrojejunal ulceration. Perhaps careful follow-up studies over the next five years will demonstrate the efficacy of combining gastroenterostomy with infradiaphragmatic vagotomy in either reducing or eliminating the incidence of gastrojejunal ulceration. Until then we shall continue to perform subtotal gastrectomy as the operation of choice for duodenal ulcer. We shall combine it with infradiaphragmatic vagotomy, especially in those patients whose preoperative free acid studies are high, and those in whom bleeding without pain was the outstanding symptom, two categories in which recurrent gastrojejunal ulceration occasionally occurs. We have combined the procedures in 26 cases without undue risk to patients. The postoperative course has been uneventful, and up to the present there have been no difficulties ascribable to delayed gastric emptying. With the elimination of both the vagal and hormonal phases of gastric secretion, an anacidity is usually produced and, under such conditions, recurrent jejunal ulcer and hemorrhage should not occur. It is also possible that the incidence of the dumping syndrome, so distressing to some patients, may be lessened. However, final comment must await adequate follow up.

The most striking benefits following severance of the vagus nerves are seen in patients suffering from gastrojejunal ulceration. In four cases of gastrojejunal ulcer following gastroenterostomy and in 11 cases following subtotal gastrectomy, excellent immediate results following vagotomy have been observed. In these patients the excruciating abdominal pain was immediately relieved, the free gastric acidity was either materially reduced in quantity or an anacidity was produced, and the jejunal ulcers which were previously demonstrated by x-ray with barium rapidly disappeared. The postoperative course was not marked by any gastric disturbances. Up to the present, 12 cases have remained well and

in three patients there have been recurrences, but in these cases the insulin test revealed that the vagus nerves were incompletely divided

The problem of gastric ulcer is another important consideration I regret that I did a supradiaphragmatic vagotomy in one case, although the ulcer disappeared and the patient has remained well The surgeon is never absolutely sure that an ulcer of the stomach is not malignant The only safe method is the radical removal of the lesion for pathologic examination by subtotal gastrectomy The clinical results of that procedure have been uniformly regarded as excellent over a twenty year period, and there is no reason to discard subtotal gastrectomy if there is even the remotest possibility that a vagotomy may be performed for an unsuspected malignancy

TABLE I  
SUMMARY  
*33 Cases Treated by Supradiaphragmatic Vagotomy*

No of Cases	Diagnosis	Predominant Symptom	Results
20	Duodenal ulcer	3—Bleeding—1½ to 7 yrs 17—Intractable pain—1½ to 25 yrs	8—Well—6 to 12 mos 7—Motility disturbances—lasting 1 to 10 mos 4—Motility disturbances—6 to 8 mos Requiring surgical therapy 1—Persistent ulcer pain—2 mos Requiring surgical therapy
1	Gastric ulcer	Pain—4 yrs	Well—12 mos (Motility disturbances 5 mos)
10	Gastrojejunal ulcer following subtotal gastrectomy for duodenal ulcer	1—Bleeding—1½ yrs 9—Pain—4 mos to 6 yrs	4—Well—6 to 18 mos 2—Improved—11 to 14 mos *2—Recurrences of bleeding—13 mos postoperative 1—Recurrence of pain—10 mos postoperative 1—Death—14 days after operation (hemorrhage into left adrenal gland)
2	Gastrojejunal ulcer following gastroenterostomy for duodenal ulcer	2—Bleeding—6 to 9 yrs	1—Well—17 mos 1—Well—7 mos (Motility disturbances 2 mos)

\* One case previously reported in Tr Am Surg Assn Vol LIX, 1941 p 334

DR FRANK H LAHEY, Boston These papers represent a very fair presentation of what is going on with vagotomy I want to present one thing unfavorable to subtotal gastrectomy, and the relation of vagotomy to it, based upon our experience with it The members of our gastroenterologic department have been studying patients who have had bleeding after subtotal gastrectomy done for a bleeding duodenal ulcer Of 100 patients having duodenal ulcer who have had subtotal gastrectomy with hemorrhage as the indication for surgery, and in whom the subtotal gastrectomy was at a very high level and the bleeding ulcer removed in every case, 28 have bled postoperatively Although only five of these patients were proved to have jejunal ulcer, it seems reasonable that the remainder must have had at least some mucosal ulceration to have produced the bleeding Many of these patients have not bled again and are perfectly well, but this is a disturbing percentage of bleeding cases after subtotal gastrectomy for bleeding duodenal ulcer

When we have a group of 28 patients with postoperative bleeding out of 100 with partial gastrectomy, we believe that anything that can be added to make the operation more aggressive should be done We therefore believe that in all subtotal gastrectomies done upon patients with bleeding duodenal ulcers, infradiaphragmatic vagotomy is a valuable measure to be employed in addition to the subtotal gastrectomy, and we recommend and have employed this additional procedure

Regarding our use of vagotomy, we would not employ this procedure, as has been

done, in any patient with a gastric ulcer because of the dangers, which I have already stated in a previous discussion, of overlooking malignancy. We particularly employ vagotomy, preferably transthoracic vagotomy, for jejunal ulcers which have occurred after subtotal gastrectomy. We would employ vagotomy for duodenal ulcers at or below the entrance of the common duct into the duodenum, and for those occasional low duodenal

TABLE II  
RECURRENCES FOLLOWING SUPRADIAPHRAGMATIC VAGOTOMY

Case	Preoperative Diagnosis and Symptoms	Date of Vagotomy	Postoperative Symptoms	Date of Abdominal Exploration		Operative Procedure
J R 547866	Duodenal ulcer Pain—4 yrs	5/ 2/46	Vomiting Foul eructations Pain	12/12/46 7 mos	Ulcer—Healed Pylorus—Patent Stomach—Slightly dilated Colon and duodenum —Dilated	Exploration only
R H 548657	Duodenal ulcer Pain—6 yrs	5/16/46	Vomiting Foul eructations	1/ 9/46 7 mos	Ulcer—Healed Pylorus—Patent Stomach—Twice normal size	Subtotal Gastrectomy
A J 548450	Duodenal ulcer Pain and vomiting 25 yrs	5/16/46	Vomiting Foul eructations	10/28/46 5 mos	Ulcer—Healed Pylorus—Patent Stomach—Dilated	Subtotal Gastrectomy
A A 549604	Duodenal ulcer Pain 1½ yrs	6/ 3/46	Vomiting Foul eructations Pain	12/ 2/46 6 mos	Ulcer—Healed Pylorus—Patent Stomach—Dilated and flabby Scar of old gastric ulcer	Subtotal Gastrectomy
W K 547393	Duodenal ulcer Pain—1½ yrs	5/13/46	Vomiting Pain	7/ 8/46 2 mos	Ulcer—Active Pylorus—Moderate stenosis Stomach—Normal	Subtotal Gastrectomy

TABLE III

## SUMMARY

## 44 Cases Treated by Infradiaphragmatic Vagotomy

No of Cases	Accompanying Procedure	Diagnosis	Results
3	Vagotomy only	Gastrojejunal ulcer 2—After gastroenterostomy 1—After subtotal gastrectomy	Recent
15	Gastroenterostomy	Duodenal ulcer	1 Died from secondary jejunostomy (peritonitis) 1 Well—14 mos 13 Recent
26	Subtotal gastrectomy (1 prepyloric exclusion)	24 Duodenal ulcer 2 Gastrojejunal ulcer after gastroenterostomy	6—Well—5 to 17 mos 1 Improved—11 mos 19 Recent

ulcers so adherent to the common duct that we do not believe they could be resected safely. We know from our own experience that there are rare duodenal ulcers occurring in the duodenum below or at the level of the entrance of the duct in which, if resection were done, transplantation of the common and pancreatic ducts, as we have occasionally done, would be necessary. We would in addition like to select a series of uncomplicated duodenal ulcers in which we could do a transthoracic vagotomy without the need of other complicating

operations such as gastroenterostomy, with the hope that we could eventually interpret for ourselves the value of this procedure in this group of patients in whom but a single procedure (vagotomy) has been applied

DR PAUL H THORLAKSON, Winnipeg I belong to the group of surgeons who have observed this new procedure with considerable hope but with some skepticism May I summarize, without comment, the experience at the Winnipeg Clinic in 39 cases of gastric, duodenal and marginal ulcers subjected to vagotomy My associates in the department of surgery, Dr M B Perrin and Dr K R Trueman, working in collaboration with Dr J W Macleod of the department of medicine, are chiefly responsible for the selection of cases and for the pre- and postoperative studies as well as the surgical procedure in this series The series began in May, 1946, and includes those treated up to February of this year

Our series consists of 39 cases with no mortality Thirty-three underwent intrathoracic and six subdiaphragmatic vagotomy The ages varied from 21 to 59 years There were five women and 34 men in the series Thirty-four of the patients had duodenal ulcer, two had gastric ulcers and two had marginal or stoma ulcers Seven of these patients had had previous gastroenterostomies

The immediate results have for the most part been unusually satisfactory Certain early difficulties have been reduced as our experience has increased

There has been in all cases after the operation relief of ulcer pain Obviously it is too early to know how permanent this may be The great majority have felt well and have gained weight There has been a very appreciable improvement in their outlook on life The ulcer craters have healed in a relatively short time as demonstrated by x-ray studies Gastric acidity has been reduced and in some there is an achlorhydria However, in some there has been a response to the insulin hypoglycemia test, indicating the possibility of surviving intact vagus nerve fibers

A number of postoperative conditions have been encountered In 21 cases fluid was present in the chest, as evidenced clinically or by x-ray film In only seven was it necessary to require aspiration Several of these latter had a troublesome cough and severe pain in the chest, which were considerably relieved by aspiration of the fluid Dysphagia was a complaint in five instances, the difficulty was for the most part temporary, although esophagoscopy was resorted to in one patient to provide relief as well as to investigate the possibility of damage Diarrhea has occurred in four cases It has not been serious and tends rather to be intermittent Most cases have shown some gastric retention after surgery and in three it has been marked A most stubborn case was advised to have gastroenterostomy for relief, but the patient refused A recent advice from him indicates that he has felt well and gained weight

One patient, having a large gastric ulcer of long duration, showing an atonic stomach and prolonged emptying time, still has her ulcer, decreased in size, but present

Two cases with duodenal ulcer have their ulcers at the present time, one is a recurrence and one has not healed in six months Both these cases showed acid response to insulin injection postoperatively These may be cases of incompletely sectioned vagus nerves, it is possible some fibers enter the wall of the esophagus and cannot be seen or felt at the time of operation

At the present time it is our feeling that the delayed emptying of the vagotomized stomach does not constitute such a problem that gastroenterostomy should be performed routinely By such a combination of procedures one cannot correctly evaluate a method of therapy which by itself appears to possess much merit

DR WILLIAM DEW ANDRUS, New York I should like to introduce into this discussion a report of physiologic studies which, while made on a single patient, have shown certain interesting effects of vagotomy

The patient was a man about 50 years of age who entered the hospital with almost complete obstruction of the esophagus due to carcinoma. The size and extent of the growth above the arch of the aorta made it appear from the x-ray that the growth was inoperable, or if operable that a complete resection of the thoracic esophagus would be required. A gastrostomy of the Glassman type was therefore performed for feeding purposes and in order to permit more direct observations on gastric function, Dr Stewart Wolf then collaborated with us in making extensive studies on this patient, similar to those made with Dr Harold Wolff on "Tom", a man with a permanent gastrocutaneous fistula. While because of anacidity it was not possible to study the secretion of acid in this patient, a variety of other studies were carried out, among them investigations of the effects of emotion on the gastric mucosa.

It happened that this patient felt very resentful about the way his case has been handled by a certain doctor before the diagnosis was made, and when questioned about his treatment before entering the hospital his face would become flushed and he would swear and show other evidences of extreme resentment and anger. During such an episode the gastric mucosa observed through the gastrostomy would become very engorged and red, showing changes identical with those seen by Wolff and Wolf in "Tom" under similar emotional stress. These studies were carried out on several occasions before exploratory thoracotomy was performed. At the time of this operation the growth was found to involve the aortic arch and the surrounding structures to such an extent as to be inoperable. A supradiaphragmatic section of the vagus nerves was, however, carried out and after about two weeks had elapsed the pre-operative studies of gastric physiology were repeated. The most striking finding was the fact that episodes of resentment now, while they were associated with flushing and external signs, no longer produced any changes in the gastric mucosa.

These studies suggest that after vagotomy the changes in the gastric mucosa associated with certain emotions such as the turgescence which has been shown to lead to increased susceptibility to superficial erosion or injury, may be eliminated.

DR EDWIN M. MILLER, Chicago. One would be bold to attempt to add very much to this very instructive symposium, but one statement can be made, I am sure, without fear of contradiction, i.e., that this work of Dr Dragstedt and his associates has brought before the public a topic that has provoked more discussion and more argument than any in the entire field of surgery in recent years. Not only does this apply to meetings where doctors are gathered together, but to gatherings of lay people as well, especially where doctors' wives are present, or patients suffering from peptic ulcer. One can also, in the mind's eye, see innumerable examples over this country of small family gatherings where one member has had an ulcer, and as a result all of them have become more or less familiar, either through the daily newspaper, literary digests, or medical magazines, with this new treatment for the disease. This widespread publicity will doubtless in the long run be a good thing, yet temporarily it may be detrimental to progress in this field. There will be many doctors who will be carried away by the general enthusiasm, will be over-zealous in performing these vagus nerve operations, with insufficient indications, without adequate preoperative study, without technical ability, and who have not the laboratory facilities for making careful postoperative follow-up studies. As a result, inaccurate observations may be published, and the true worth of vagus nerve sections in the treatment of chronic peptic ulcer may not be determined for a long time.

We hesitate at this time to make any definite statements about results in our own cases, first, because the series (15 personal cases and 25 others) is very small, second, because the elapsed time since our first operation has been too short. However, we can with certainty say that we are thus far very favorably impressed with the progress of our patients. We have preferred the transthoracic approach, because our anatomic studies have shown us that a more accurate dissection can be made through the chest, and therefore the chance of leaving behind undivided vagus nerve branches is minimized. Yet

we acknowledge the necessity of the abdominal route when the need for a gastroenterostomy is present

Our postoperative complications have been few in number, minor in degree, and temporary in duration. Among them may be listed cardiospasm, pylorospasm, delayed emptying of the stomach, pain in the chest, mild paralytic ileus, and diarrhea. A more definite statement can be made after much more time has elapsed.

DR R. KENNEDY GILCHRIST, Chicago. I have heard this discussion three times, and there is one question I would like to have answered. It seems that we have intestinal upsets after surgery. Before surgery, there is high acidity, and after surgery, no acid is present. Also, there is very much delayed emptying time of the stomach. With the absence of acid, this establishes a perfect culture medium. It seems that one of the most common complications is diarrhea. I would like to know how much work has been done on the question as to whether there is a change in the flora of the stomach, or whether some peculiar flora is present which, when the contents of the stomach are emptied into the intestine, causes the diarrhea.

DR HAROLD M. WOOKLY, Toronto. I have listened with a good deal of interest to the symposium on the effects of vagotomy on the function of the stomach and to its application in the treatment of peptic ulcer. It has been suggested that the full beneficial effects of this procedure would not occur unless all the vagus fibers were included. I have found that the esophagus and vagi are more easily reached by a rightsided approach through the thorax. The vagi may then be divided at a higher level and in this way one would be more certain that all fibers proceeding to the stomach are included. In my opinion, this is a simpler operation and less disturbing to the patient.

DR OWEN H. WANGENSTEEN, Minneapolis. As physiologist and surgeon Dr. Dragstedt has made contributions of the greatest importance to our understanding of gastric physiology. I am certain that surgeons and physiologists generally are awaiting with keen interest the outcome of this new venture of Dr. Dragstedt in attacking the problem of ulcer by the performance of complete vagus section. In our clinic, there is an intense interest in the ulcer problem, both in the hospital and in the laboratory. With reference to the question of vagotomy, however, we have felt this is a problem which should be threshed out in a few areas. Yet in my community, a number of surgeons in the Twin Cities who had never explored the possibilities of resection are performing vagotomies in large numbers. In January, Dr. Walters and his associates from Rochester presented their material on vagotomy. His results suggest definitely that vagotomy does not consistently afford patients with ulcer that degree of protection which one would like to find in an operative procedure. As a matter of fact, following Dr. Walters' talk on vagotomy for ulcer in St. Paul, it was to be noted that all the lobby telephones were busy. Internists and surgeons alike probably were already cancelling vagotomies that had been scheduled. In any case, in my area, the enthusiasm for vagotomy has been dampened perceptibly by the report of Dr. Walters and his colleagues.

It would be very helpful indeed if an experiment could be devised by which the protection afforded by vagotomy against the ulcer diathesis could be tested critically. Pavlov showed that vagotomy ablated the cephalic or psychic phase of gastric secretion. Moreover, Dr. Dragstedt has shown that vagotomy has a profound depressing influence on gastric secretion in man. Vagotomy, however, does not impede humoral stimuli of gastric secretion. And in dogs, whereas there is an early depression of gastric secretion following vagus section, with the elapse of time there appears to be a fairly complete recovery viewed from the over-all response to a meat meal\*.

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\* Discussion of Dr. L. R. Dragstedt's paper "Section of the Vagus Nerve in Treatment of Gastrojejunal Ulcer" *Minn. Medicine*, 21: 604, 1946.



Vagotomy fails to protect against the histamine-provoked ulcer in the dog (Ivan D Baronofsky, Stanley Friesen, Enrique Sanchez-Palomera, Frank Cole, and Owen H Wangensteen 62 114, 1946) Obviously, there is no real antithesis between vagotomy and histamine, for histamine will stimulate the parietal cells after vagotomy Hence, Dr Dragstedt justifiably may object to testing the protection afforded by vagotomy against the histamine-provoked ulcer However, the very circumstance that vagotomized patients will not be protected against humoral influences such as food, caffeine and alcohol, which stimulate the parietal cells to secrete hydrochloric acid, suggests that vagotomy may prove an inadequate protection against the ulcer diathesis of man Even in dogs, vagotomy will retard the histamine-provoked ulcer but it will not preclude its occurrence My associates and I are trying to determine in the laboratory whether vagotomy will protect against some of the abetting causes of ulcer It will be particularly interesting to try to determine whether vagotomy will abolish the ulcerogenic effects of tension-states My associate, Dr Walter Lillehei, is accumulating some interesting data on the effects of stimulating the extrinsic nerves of the stomach as well as on the effects of removal of its extrinsic nerve supply Sympathectomy definitely abets the ulcer diathesis in dogs and we might reasonably assume that some patients who have undergone sympathectomy for hypertension may develop ulcer Vagotomy, on the contrary, does exhibit a retarding effect on the development of ulcer The extent of this delaying or retarding influence remains to be determined

When a patient with an ulcer submits to operation for its correction, he may rightfully expect protection from ulcer recurrence That, however, has been the great weakness of operations devised to rid a patient of the ulcer diathesis We surgeons have been too empirical in our approach to this problem Dr Dragstedt's medical associate, Dr W L Palmer, is author of the statement that 40 per cent of patients for whom gastrojejunostomy was performed for duodenal ulcer at the University of Chicago Clinics developed gastrojejunal ulcer\* That gastrojejunostomy sensitizes a dog to the occurrence of gastrojejunal ulcer is well known\*\* This circumstance is even more evident in dogs receiving histamine-in-beeswax after gastrojejunostomy, ulcer occurs much more readily than it does in the dog that has not undergone gastrojejunostomy

The wisdom of adding gastrojejunostomy to vagotomy to thwart the ulcer diathesis in man is therefore a debatable matter

DR R ARNOLD GRISWOLD, Louisville, Ky (closing) My personal experience with vagotomy is limited to 34 cases I will simply say that the results have been satisfactory to us and to the patients, with about the same ratio of good results and side effects as presented by the other speakers In addition to the chemical work Dr Schoen has done, we have been interested in the psychiatric side of the ulcer problem Dr Arthur Benton of the University of Louisville Mental Hygiene Clinic, has been doing psychologic tests including the Rorschach test and the Minnesota multiphasic personality inventory on these patients before and after operation All patients tested preoperatively showed more or less severe degrees of psychologic disturbance The majority showed emotional constriction, a pattern usually associated with severe psychoneurosis Others showed the type of performance often found in chronically maladjusted, aggressive individuals who show evidence of hostile and (using the term in a broad sense) paranoid attitudes Since vagotomy may be considered as separating the soma from the psyche, we have been interested in repeating these tests postoperatively So far, in the small number of individuals tested, postoperative tests have shown no psychologic change due to relief of the ulcer symptoms They are still the same emotionally disturbed individuals as they were before operation Tests will be continued at a later date following operation, since the average postoperative test so far has been about two months postoperative

\* Journal-Lancet, 62 415, 1942

\*\* Montgomery, A H Gastrojejunal ulcer, an experimental study, Arch Surg, 6 136, 1923

Concerning the question of operative approach, we have favored the thoracic exposure because of the greater ease, facility and certainty of dividing all vagal fibers, as well as the lessened morbidity following this approach. Of course, in those cases in which a drainage operation is necessary, or in which it is felt necessary to visually and manually examine the pathology, the abdominal approach has been used. We have used the abdominal approach in about 25 per cent of our cases. Routinely, I do not think it makes much difference. It is a minor problem, such as whether you remove a gall-bladder from the fundus down or the cystic duct up. The surgeon who is more familiar with abdominal surgery than with thoracic surgery will probably always prefer the abdominal approach. I do not think it is a matter of much importance.

DR. FRANCIS D. MOORE, Boston (closing) I would like to thank the essayists and discussors for a most instructive afternoon. One point should be emphasized that I did not stress before, namely, that one year after vagus resection the fasting acidity and motility of the stomach have readjusted themselves to denervation and returned to essentially normal values. I am not referring to overnight suction experiments such as Dr. Dragstedt has studied, but rather to serial determination of the titratable acidity and pH of the secretion. The "psychic phase" is doubtless still abolished and the insulin curves remain "flat." However, we should not lose sight of the fact that a year after vagus division titratable free acidity in the stomach is often 20 and 50 units and a pH between 1 and 2. We should therefore not refer to vagus division as an operation which lowers gastric acidity. It produces a temporary change in fasting acidity, and doubtless a permanent change in acidity produced in response to cortical stimuli.

As to the fibers which have been found in the wall of the esophagus, I am quite puzzled as to the proper interpretation of these data. We dissected a good many cadavers before we carried out our first human operation, and in all of these we found fibers of the vagi in the esophageal wall. These fibers, which are occasionally fairly good size, ran down and ended for the most part in or just below the cardiac orifice. We interpreted them as motor fibers to the muscular wall at the junction of esophagus and stomach. I would not feel convinced that sectioning one of these small fibers had accomplished much change in the physiologic conduct of the rest of the organ.

As for doing this operation with subtotal gastrectomy, I have shuddered when this has been mentioned as a routine procedure. It did not seem justified to subject a large group of patients to the side effects of vagus division when they were already having an operation carried out which has its own imposing list of by-products. However, there may remain a special group of cases such as Dr. Lahey mentioned in which the combination is justifiable.

We operate through the chest purely for anatomic reasons, feeling that we do a better job.

Although vagus resection is in a very difficult phase to evaluate I think that it is going to work itself into the overall picture in a fashion analogous to splanchicectomy for hypertension. In both situations we have varying combinations of local, humoral, neurogenic, and environmental factors responsible. The nerve-dividing operation controls only those patients in whom nerve-mediated factors are of outstanding significance. I would never expect 100 per cent good results from this operation if applied to an unselected ulcer population. The reason for this is that in a large group of ulcer patients these various etiologic mechanisms are at work in varying combinations. I think the final solution of our problem is going to come when, by careful research, we learn how to select those patients in whom the nerve-mediated factors outweigh in importance the other ulcer-producing mechanisms.

DR. WALTMAN WALTERS, Rochester, Minn (closing) In answer to Dr. Gilchrist's question, is it not likely that one cause for the diarrhea is jejunitis, which is found in some who have had persisting symptoms. In nine dogs in whom the Mann-Williamson

ulcer was produced, Saltzstein and Sandwiss found severe jejunitis present in six. These dogs had diarrhea. Bacterial contamination of food remnants remaining in the stomach as a result of gastric stasis from atony is another possibility, as Dr. Gilchrist has mentioned.

DR. LESTER R. DRAGSTEDT, Chicago (closing) I should like first to refer to Dr. Wangenstein's comment. We are greatly indebted to him and to his associates for one of the most significant experiments on the pathogenesis of peptic ulcer. He demonstrated that if an excessive, continuous secretion of gastric juice is produced and maintained in experimental animals, peptic ulcers regularly develop. This excessive gastric secretion was produced by implanting pellets of histamine and beeswax into the subcutaneous tissues. The gradual absorption of histamine from these pellets provided a long continued chemical stimulation of the gastric glands in the intervals between meals. I am not surprised at Dr. Wangenstein's statement that these histamine ulcers can be regularly produced in animals even after division of the vagus nerves. So far as we know, histamine acts chiefly locally on the neuroglandular apparatus in the stomach and not on the brain. Section of the vagus nerves, therefore, should not interfere with the secretory effect of the absorbed histamine. I should like to emphasize again that in patients with peptic ulcer, the excessive, continuous secretion of gastric juice is neurogenic in origin and is abolished by division of the vagus nerves to the stomach. The excessive, continuous secretion of gastric juice produced by the implantation of pellets of histamine and beeswax into the subcutaneous tissue, on the other hand, is chemical in origin and should not be abolished by sectioning the vagus nerves to the stomach. The situation in the two cases is, therefore, not comparable.

Early in our work with gastric vagotomy in the treatment of peptic ulcer, we were impressed with the profound decrease in tonus and motility of the stomach which follows this operation. It is important, however, to realize that whereas the motility is reduced, it is not abolished, and that after a time, a readjustment in the peripheral automatic motor mechanism of the stomach takes place so that the gastric movements return toward the normal state. In the interval, however, the stomach is very susceptible to the dilating effect of swallowed air and accumulated secretion. Overdistention of the stomach at this time markedly delays the resumption of normal motility through the agency of Auerbach's plexus. It is our usual practice to decompress the stomach by means of the Wangenstein apparatus for five days following the vagus section, then allow small amounts of water, and subsequently aspirate the stomach to determine if retention has occurred. Only when liquids empty readily do we allow solid food. The patients are carefully instructed not to overload the stomach for the first few months following the operation. The dietary restriction is thus quantitative rather than qualitative in nature.

I was very much interested in Dr. Moore's statement that within a year following section of the vagus nerves to the stomach, the secretion of gastric juice and motility return to the preoperative level. In our experience, section of the vagus nerves has abolished permanently the nervous phase of gastric secretion. I think this is most important. Up to the present time, we have secured no evidence of regeneration of the secretory fibers in the vagus nerve to the stomach as determined by physiologic tests. The usual failure of the recurrent laryngeal nerve to regenerate following damage in thyroid surgery is of interest in this connection. While the period of clinical observation is still too short for us to know whether or not recurrence of these ulcers that have healed following vagus section will take place, the data from the experimental laboratory permit us to be quite optimistic. I do not believe that these ulcers will recur unless the vagus nerves regenerate and the excessive, continuous secretion of gastric juice of nervous origin is resumed. Since regeneration of these nerves has not been seen even in the patients operated upon four years ago, it seems unlikely, on the basis of what we have learned about regeneration of nerves elsewhere, that this will take place.

# ABDOMINAL VISCERAL SENSATION IN MAN\*

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THE RECOGNITION of the existence of visceral pain has been comparatively recent. Before and for some years after Langley's<sup>1</sup> (1903) review of the functions of the autonomic nervous system it was believed that such afferent fibers as were known to accompany autonomic nerves served only in reflex mechanisms to autonomic tissues and were "incapable of directly giving rise to sensation." Ross<sup>2</sup> in 1887 had shown that tension in a hollow viscus produced pain that was perceived in a corresponding cutaneous dermatome on the abdominal wall. But Lennander<sup>3</sup> (1902) as a result of observing the lack of pain when the bowel was cut or otherwise traumatized concluded that the bowel was insensitive to painful stimuli and that any pain accompanying visceral stimulation resulted from irritation of the pain sensitive parietal peritoneum. It was not until 1911 that Hurst,<sup>4</sup> employing balloon distention of the bowel, demonstrated conclusively in man that sensation from the bowel could be elicited and emphasized the need for employing an adequate stimulus in studying visceral sensation.

Stimulation of the parietal pleura or peritoneum by friction or faradism results in pain, the impulses travelling via somatic afferent fibers in spinal nerves. But visceral pleura and peritoneum have been found insensitive to similar stimuli, and most observers have likewise found the mucosa of the stomach and bowel to lack pain sensitivity<sup>5, 6, 7</sup>. The stimulus adequate for the production of visceral pain is believed by many to be traction on the mesenteries, and Alvarez<sup>6</sup> states that neither distention nor contraction of a hollow viscus causes pain unless the adjacent mesentery is stretched. On the contrary, others<sup>8, 9</sup> believe that pain which results from distention of a viscus is due to stretching of its sensory nerves, while Huist<sup>4</sup> and Ryle<sup>10</sup> contend that tension of the muscular coat or a distended or contracted viscus provides the stimulus for pain.

Many analogies can be drawn between somatic and visceral pain but certain striking differences are important to recognize for purposes of clinical investigation. Somatic pain which is conducted by spinal nerves has the property of sharpness and accurate surface localization which is largely acquired after birth, while visceral pain on the contrary is deep, dull and less well localized. But sometimes there may be a supplementary mechanism by which visceral pain is referred to a cutaneous region which has a corresponding segmental innervation. Sometimes this referred pain has been looked upon as the sole manifestation of visceral pain but blocking of the painful area locally

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or interruption of the spinal nerves supplying the area by procainization cannot be counted on to abolish visceral pain<sup>11</sup>

The matter of the types of end organ for visceral pain reception and their exact location is still unsettled. Tyrrell-Gray<sup>12</sup> (1922) advanced the view that the afferent end organs were the Pacinian corpuscles occupying the mesentery and that they responded to mechanical, thermal, chemical and electrical stimuli. Sheehan<sup>13</sup> (1933) summarized his studies of degeneration following section of the vagi and sympathetics by concluding that visceral pain in the abdomen arises from mesenteric nerve endings of 3 types: (1) Pacinian Bodies, (2) free endings of myelinated nerves and, (3) free endings of a fine plexus of non-myelinated fibers. The Pacinian corpuscles were found to be distributed to the mesentery of the bowel chiefly around large vessels but not in the bowel wall, and in the pancreas and about the biliary tree but not in the omentum. Splanchnicectomy resulted in degeneration of the Pacinian corpuscles.

The vagus nerves possess afferent fibers which are believed to conduct certain reflex stimuli from the abdominal viscera but not pain sensation (Cannon<sup>14</sup>). While some still doubt that the vagus nerves do not transmit pain impulses from abdominal viscera, almost all investigators agree that the splanchnics and other sympathetic nerves do possess visceral pain fibers. The axones of the visceral afferent nerves accompanying the sympathetic nerves are poorly myelinated and their rate of conduction is slow. They run all the way to the cord without synapse and enter via the posterior spinal roots. Earlier contention that visceral afferent impulses traversed anterior spinal roots<sup>15</sup> has been largely discredited by later work such as that of Davis, Pollock and Stone<sup>11</sup> which concluded that visceral afferents enter the cord only by the posterior roots.

A table of the segmental sensory innervation of the viscera was compiled by White and Smithwick<sup>16</sup> (1941) from available experimental and clinical data, but much of the evidence is of necessity inferential. On the whole, comparatively few observations have been made in man on the pathways for the conduction of visceral pain. Efforts to map the spinal segments which transmit painful sensations from various levels in the gastro-intestinal tract by paravertebral injection of anesthetic agents have been described by Lawen<sup>17</sup> and by Kappis and Gerlach.<sup>18</sup> Adson<sup>19</sup> (1935) and Leriche<sup>20</sup> (1937) stimulated the splanchnic nerves in the course of operations performed during spinal anesthesia and produced pain in the upper scapular region on stimulation of the greater splanchnic, and pain lower down on stimulation of the lesser nerve. White<sup>21</sup> (1943) reviewed the sensory innervation of the viscera in man based on neurosurgical procedures performed for the relief of intractable pain and added an account of his own experiences.

Conclusions drawn from the results of somewhat blind injections of anesthetic agents about unseen nerves usually leave some doubt and the aggregate of experiences with alteration in visceral sensation after surgical interruption of visceral afferent nerves is relatively meager and inconclusive. For example, pain sensation originating in the heart and in the urinary bladder has received

greater attention than almost any other form of visceral sensation, yet the information is incomplete. Sympathectomy<sup>16, 22</sup> and posterior rhizotomy<sup>23, 24</sup> for relief of cardiac pain have effectively demonstrated afferent pathways through the upper 5 thoracic sympathetic ganglia and posterior roots but leave unexplained the residual pain in the neck which occurs in some patients. Learmonth's<sup>25</sup> investigations of bladder sensation indicate the role of visceral afferent fibers in the triple innervation of the bladder but leave unanswered the detailed pathway of the sensory fibers accompanying the sympathetic nerves.

The present study was carried out on a series of patients most of whom had hypertensive cardiovascular disease and all of whom were subjected to thoracolumbar sympathectomy in which the paravertebral ganglionated chain was resected from the seventh thoracic through the third lumbar ganglia, and the splanchnics were resected from the celiac ganglia to a point above the contribution of the seventh thoracic ramus. In certain studies additional interruption of nerve pathways supplemented the standard sympathectomy. Observations were made on the pain sensitivity of the stomach, large and small intestine, biliary tree, pancreas and urinary tract prior to denervation, and at various times up to one year after right or left sympathectomy and after bilateral sympathectomy. Such tests are tedious and try the patience of both the subject and the examiner. The use of the tests and interpretation of the results require circumspection. All of the results to be reported have been observed more than once and in some cases many times, and while it is realized that additional observations are desirable the findings seem adequate at least for a preliminary report.

#### BALLOON DISTENTION OF THE INTESTINAL TRACT

Fifteen patients were selected for this study. A rubber bag attached to the end of a Miller-Abbott tube was passed through the mouth to various levels in the intestinal tract and the position of the bag identified by fluoroscopy.

The main cavity of the stomach because of its size and the distensibility of its wall does not lend itself readily to studies with the balloon and therefore no observations of pain by distention were made. However, the effects of temperature were studied (see section on THERMAL STIMULATION).

The *small bowel* was distended at numerous points from the duodenal cap to the cecum (Fig. 1). As a rule the pain thus induced was normally felt in a relatively discrete area somewhere in the midline between the xiphoid and the umbilicus, that from the duodenum was felt in the upper epigastrium, and that from the jejunum and ileum nearer the umbilicus. A volume of 50 to 75 cc. of air in the balloon producing a pressure of 1 to 1.5 centimeters of mercury was sufficient to cause a distinct but bearable deep aching pain. Distention to 90 to 120 cc. of air at a pressure of 1.5 to 2 cm. of mercury was perceived as a moderate to severe pain, while more than 120 cc. of air at 3 cm. mercury pressure caused severe and more widespread pain in the midline of the abdomen. Patients subjected to the latter pressure often became pallid,

developed a cold, clammy feeling and a desire to eructate. Pain did not occur in the back. While distention of the jejunum and upper ileum was always accompanied by pain at or above the umbilicus distention of the terminal ileum sometimes also caused pain below the umbilicus and occasionally about McBurney's point. This exceptional pain below and to the right of the umbilicus

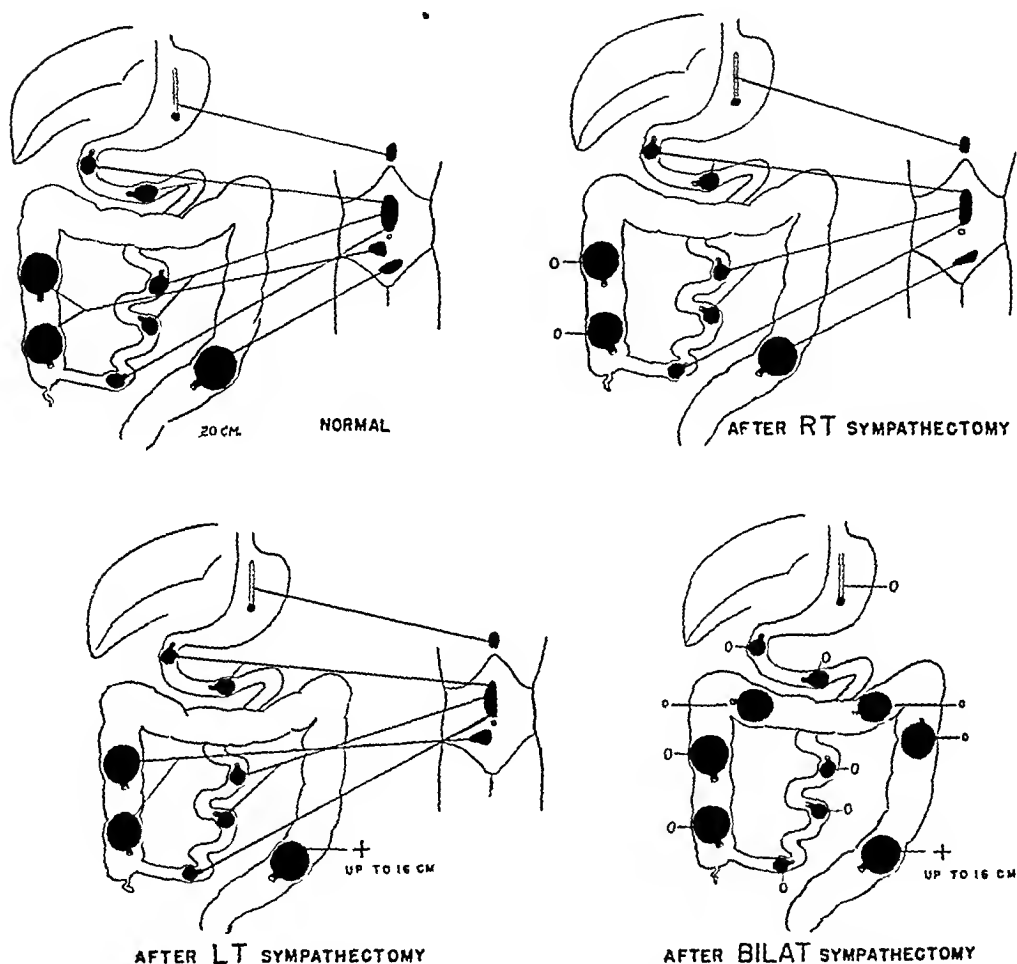


FIG 1—Balloon distention of gastro-intestinal tract. Eight areas of sensory reference.

did not have the deep aching character of the usual para-umbilical pain and could have occurred as a result of local parietal peritoneal stimulation or as a referred pain.

On repetition of the tests after either left or right sympathectomy, there was no alteration in the region at which pain was felt or in the threshold of

pain appreciation There was no tendency for lateralization of the pain to the undenervated side After bilateral sympathectomy pain could not be elicited with distention even after 300 cc of air at 4 to 6 cm of mercury pressure

The *large bowel* is less satisfactory to investigate because of the difficult and unpleasant task of passing the tube and balloon the longer distance and maintaining it for the period of time necessary for the tests However, enough observations were made to afford general conclusions About the same pressure within the balloon sufficient to cause pain in the small bowel was adequate stimulus for pain in the large bowel with the possible exception that relatively higher pressure was sometimes needed in the cecum to cause pain of comparable degree to that from 1 to 2 cm mercury pressure in the rest of the large bowel The sites of pain were relatively discrete and became more diffuse only with increased pressure within the balloon The patterns of reference are indicated in Figure 1 Normally, distention of the cecum was perceived as pain in an area just below and to the right of the umbilicus and pain arising from the hepatic flexure and proximal portion of the transverse colon occurred at points within a larger area extending from the umbilicus downward and to the right From distention of the splenic flexure and descending colon pain was felt in the lower abdomen to the left of the umbilicus, while pain from the rectosigmoid was distributed across the suprapubic region extending perhaps more to the left side In addition to tests with the balloon passed orally, several satisfactory observations on the lower bowel in its last 50 cm were made using a tube with a coil spring incorporated in a #20 French catheter passed through a proctoscope (This tube was devised by Thomas P Almy and Fred Kern of the New York Hospital)

After right sympathectomy the only alteration in large bowel sensation observed was absence of pain on distention of the cecum After left sympathectomy no alteration in large bowel sensation resulted from the studies employed although in the patients examined no satisfactory observations were made of distention of the splenic flexure and descending colon After bilateral sympathectomy the appreciation of painful distention of the large bowel was abolished above the level of 16 cm from the anus Below this level, distention of the bowel with the minimal adequate pressure still elicited pain in the suprapubic region In addition, distention of this lowest segment produced a desire to defecate

#### THERMAL STIMULATION

In normal subjects distention of a balloon in the stomach with water at temperatures of 110° to 120° F caused a feeling of heat in the subxiphoid region, while water at 32° F caused a feeling of cold in the same region Water temperatures between these extremes were not definitely perceived and one subject did not appreciate either hot or cold In 8 of 9 subjects examined after bilateral sympathectomy the ability to perceive temperature in the



stomach was abolished. In the ninth it persisted, but the area of reference before and after sympathectomy was at the sternal notch at the base of the neck. A few additional observations on thermal stimulation of the small bowel suggested that extremes of temperature are not perceived there but the evidence was incomplete.

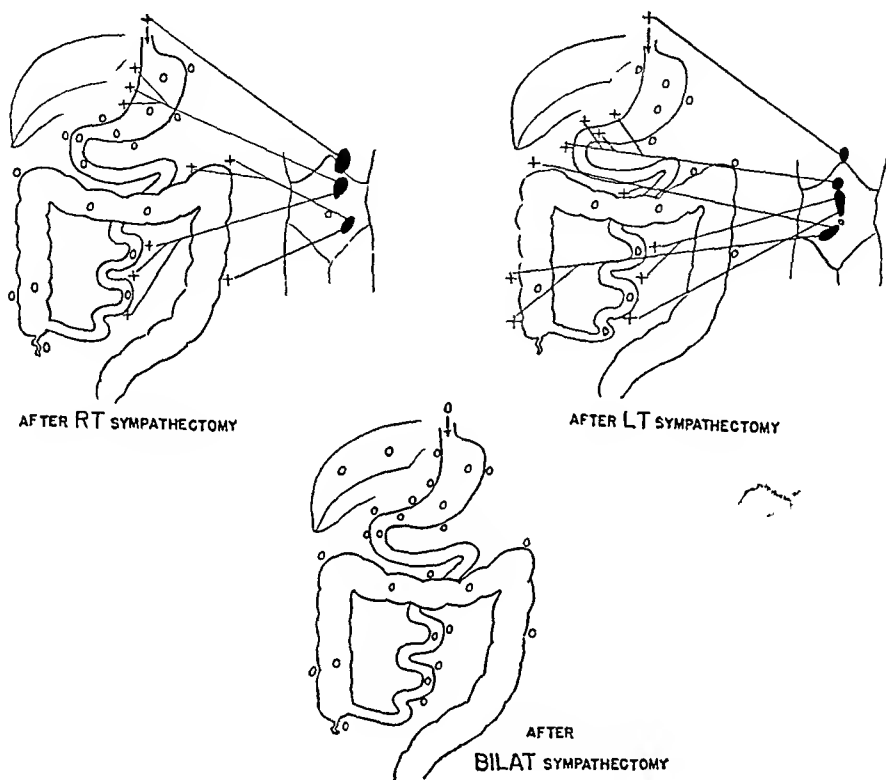


FIG 2

FIG 2—Stimulation of gastro-intestinal tract (faradic, traction stretch) through celiotomy

#### DIRECT STIMULATION OF THE STOMACH AND INTESTINAL TRACT THROUGH CELIOTOMY

The combined observations were made on 6 patients having unilateral or bilateral sympathectomy in whom some intra-abdominal operation was necessary. Regional procain anesthesia was employed only to open the anterior abdominal wall and peritoneum. The methods of stimulation employed included pinching and local stretching of the gastric and intestinal walls, traction on the mesenteries and omentum, and faradic stimulation of various structures. The electrical stimulation was performed with the Hinsey-Geohegan stimulator using a bipolar electrode and a current of between 3 to 5 volts. The results are diagrammed in Figure 2.

Even though tests were not made on unsympathectomized patients some

part of the gastro-intestinal tract was pain sensitive in the combined group of patients having unilateral (either right or left) sympathectomy. Pinching, local stretching, and faradic stimulation of the walls of the stomach and intestine failed to cause pain except at points close to the proximal mesenteric attachments. The greater curvature of the stomach, the gastrocolic omentum, and the greater omentum as well as the larger vessels they contain were not found to be pain sensitive. When any pain sensitivity was elicited along the gastro-intestinal tract it resulted from some form of stimulation of the mesentery or at the mesenteric attachment to the viscus.

*The stomach* After right sympathectomy, traction on the cardiac end of the stomach produced pain first in the left upper abdominal quadrant. As the traction was increased precordial pain, a "tugging sensation in the gullet" and nausea were added to the abdominal pain. Traction and electrical stimulation applied to the mesentery and border of the lesser curvature of the stomach along the proximal half of its extent also resulted in pain in the left upper abdomen. Similar stimulation of the pylorus and first portion of the duodenum did not elicit pain. The reverse was found in patients after left sympathectomy, *i.e.*, the proximal half of the lesser curvature and its mesentery were insensitive while the pylorus and first portion of the duodenum were sensitive, the site of reference of the pain being in a fairly discrete  $\frac{1}{2}$  in the midline and possibly slightly to the right in the epigastrium. After bilateral sympathectomy all these positive responses of pain were abolished.

*The jejunum and ileum* After unilateral sympathectomy, traction and, less constantly, electrical stimulation of the mesentery of the small bowel below the ligament of Treitz always resulted in pain in a relatively localized area above the umbilicus. After right sympathectomy the pain elicited was to the left of the midline, while after left sympathectomy the pain was in the midline or possibly slightly to the right of it. After bilateral sympathectomy no pain could be elicited from any form of stimulation of the small bowel or its mesentery.

*The large bowel* After right sympathectomy traction and, less constantly, electrical stimulation of the mesentery or adjacent portion of the peritoneum (as in the case of a retroperitoneal cecum) of the colon as far as the middle of the transverse colon failed to elicit pain. The same was true of the appendix and its mesentery. But traction of the mesentery at the splenic flexure and of the descending colon (only the upper portion was examined) resulted in pain in the right lower quadrant of the abdomen. The reverse was true after left sympathectomy in that no pain followed traction on the mesentery of the left half of the colon above the pelvic brim while traction and, sometimes electrical stimulation of the mesentery of the appendix, cecum, hepatic flexure, and right half of the transverse colon elicited pain in the right lower quadrant. After bilateral sympathectomy repetition of the tests failed to produce pain when applied to any part of the colon or its mesentery above the sigmoid.

TESTS OF PAIN SENSITIVITY OF THE BILIARY TRACT AND PANCREAS  
(FIGURE 3)

The tests were made through the open abdomen on 6 patients who had had unilateral or bilateral sympathectomy and in whom celiotomy was necessitated because of chronic disease of the gallbladder, stomach or pancreas. In addition, observations on several unsympathectomized patients were made, sufficient to establish the adequacy of the tests and to confirm similar studies made by others on normal sensation of the biliary tract. Regional procain

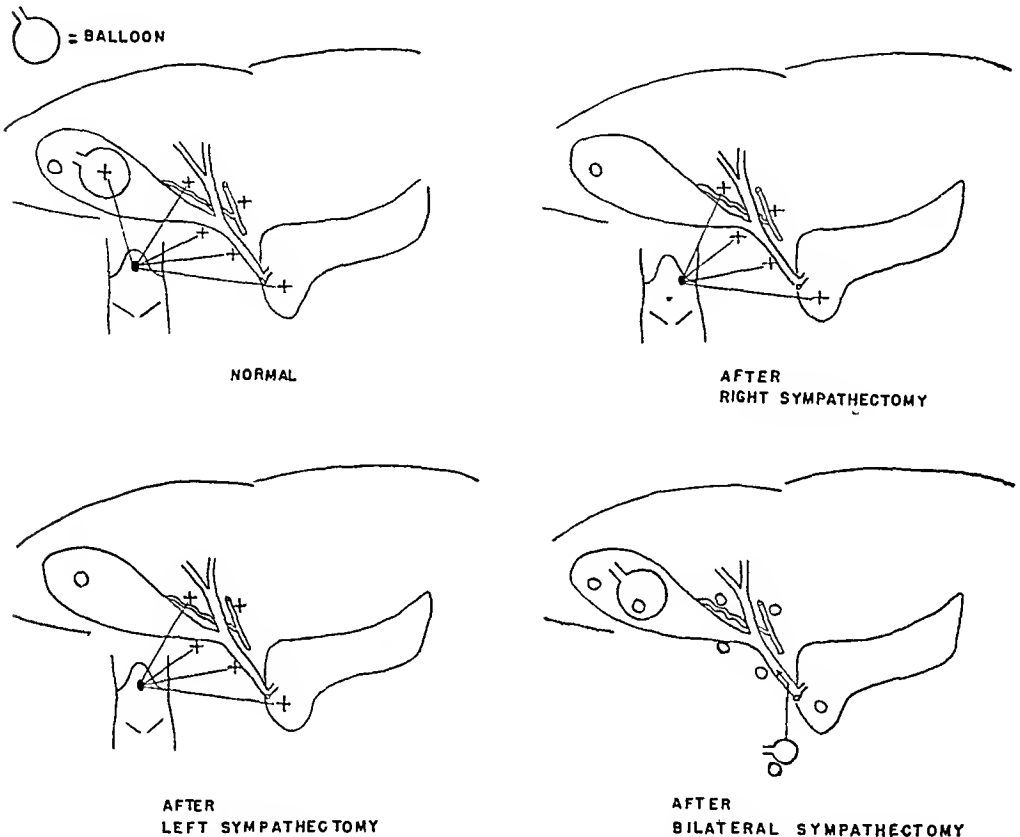


FIG 3—Stimulation of biliary system and pancreas stretch, faradic and distention

anesthesia was employed to open the anterior abdominal wall and peritoneum. The methods of stimulation employed included balloon distention of the gallbladder, distention of the common duct by saline injection, and traction and faradic stimulation (3-5 volts) of all of the extra-hepatic biliary tree, the cystic vessels and the pancreas.

In the unsympathectomized patients distention of the gallbladder by inflation of the balloon with air at 4 cm mercury pressure caused pain in a relatively small area in the midline of the epigastrium. The fundus of the

gallbladder and the capsule of the exposed liver were not pain sensitive to manipulation, local traction, or electrical stimulation. But these stimuli applied to the cystic duct, common duct, cystic artery, or head of the pancreas, each produced pain in the same spot in the mid-epigastrium. Pain did not occur in the back or in the hypochondrium.

After right sympathectomy there was no opportunity to study the effects of balloon distention of the gallbladder, but repetition of all the other tests on the biliary tract, the vessels, and head of the pancreas caused pain in the left hypochondrium. After left sympathectomy the same structures were found to be pain sensitive, but the pain was experienced in the mid-epigastrium, in addition, the pain from pressure on the head of the pancreas extended to the right hypochondrium and that from stimulation of the cystic and common ducts in one patient was experienced not only in the epigastrium but in the right infrascapular region. After bilateral sympathectomy no pain could be elicited on repetition of the tests even though the intensity of the stimuli was increased.

#### TESTS OF PAIN SENSITIVITY OF THE UPPER URINARY TRACT (FIGURE 4)

In 15 patients cystoscopic examinations before and after unilateral or bilateral sympathectomy permitted observations on pain sensitivity of the ureter. In the unsympathectomized subject mechanical irritation and faradic stimulation (3 volts) at the ureteral orifice and in the distal 6 cm of the ureter caused pain over and slightly above the symphysis pubis. Rapid injection of 10 to 20 cc of saline into the ureter (and kidney pelvis) through a #8 French ureteral catheter was very painful, the pain occurring in a broad area in the lower half of the abdomen and flank on the side stimulated. After unilateral sympathectomy the normal responses were abolished on the denervated side, there were no contralateral changes.

Two hypertensive patients undergoing sympathectomy without general anesthesia were suitably intelligent and cooperative to permit tests on the exposed kidney and upper half of the ureter. Regional procain block was used in the operative exposure of these structures and care was taken not to procainize any of the intercostal or sympathetic nerves. Faradic stimulation (up to 5 volts) of the renal capsule and pressure on the kidney at points not bordering on the renal pelvis were not painful. However pain occurred in a localized area at about the outer tip of the 12th rib on the same side when the renal pelvis, the pedicle, or the ureter near the uretero-pelvic juncture were stretched or compressed. The same type and location of pain followed faradic stimulation of these structures, including the isolated renal artery and vein. Traction and faradic stimulation of the ureter at points distal to the first several centimeters caused pain in the inguinal region on the same side. Division of the greater and lesser splanchnic nerves at the celiac ganglion and resection of the thoracic ganglionated chain from Th7 to 11, inclusive resulted in elimination of pain responses when the tests on the renal pelvis and pedicle were repeated. The pain caused

by stimulation of the ureter was not eliminated until Th12 and L1 ganglia were excised, thus extending the resection of the sympathetic chain to a point below the first lumbar ganglion

#### TESTS OF PAIN AND THERMAL SENSITIVITY OF THE URINARY BLADDER

Observations on bladder sensation in several unsympathectomized patients were made in order to establish the adequacy of the tests and confirm

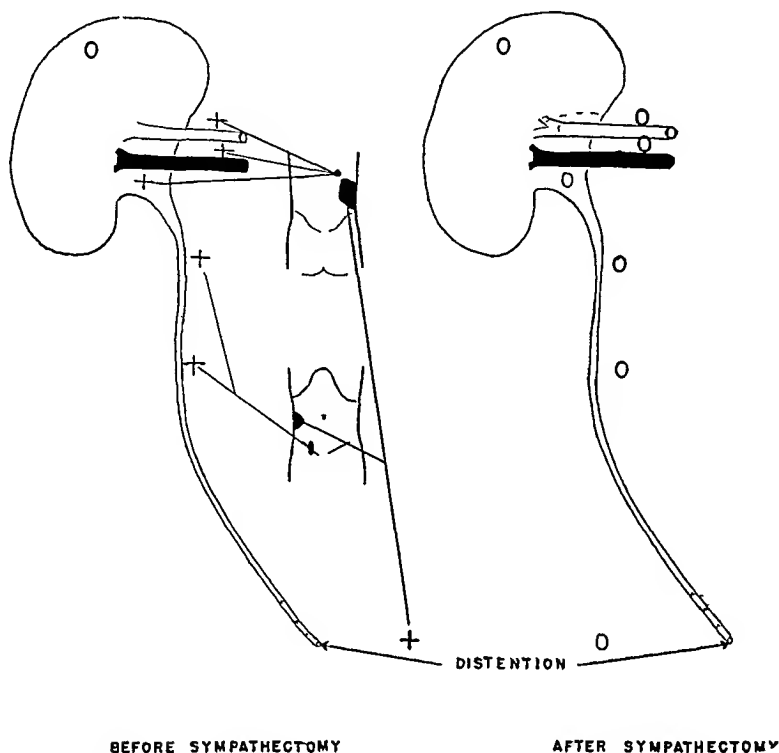


FIG 4

FIG 4—Stimulation kidney, ureter and renal vessels and areas where pain is felt

previous studies on normal bladder sensation. Faradic stimulation to the trigone (1 volt) and to the dome (2-3 volts) caused pain in the suprapubic region and over distention of the entire bladder caused similar pain. Installation in the bladder of water at 110° F was detected as warmth in the region of the pubis while water at 65° F or lower was perceived as cold in the same region. After right or left unilateral and bilateral sympathectomy, there was no appreciable change in these observations. The cystometric curve and bladder capacity were not altered from the normal after bilateral sympathectomy.

Additional light was thrown on the source of sensory supply to the bladder by studies on 2 patients who had had all sacral nerve roots (motor

and sensory) cut for relief of intractable pain due to malignant chordoma invading the sacrum. The bladder sensations resulting from faradic and thermal stimuli appeared normal both before and after the rhizotomies. There was urinary incontinence preoperatively and in both patients before and after rhizotomy there was a sense of suprapubic fullness after filling the bladder with 200 cc of water and of pain after 300 cc or more. In these patients bilateral lumbar sympathetic blocks were performed by injecting procain paravertebrally and a repetition of the tests showed that all sensation in the bladder was eliminated except a vague feeling of distress when the bladder was distended by 500 cc or more of fluid.

Since, in the two patients subjected to complete sacral rhizotomy, the visceral afferents of the bladder accompanying the parasympathetic nerves (S2, 3, 4) and the somatic sensory fibers to the pudendal nerves (S3 and 4) were all divided, no distinction between the role of these two groups of nerves was made. However, when the pudendal nerves were blocked in the perineum by procainization in patients previously subjected to bilateral sympathectomy normal bladder responses to the standard stimuli still existed. In these patients it was assumed that the only fibers remaining to transmit sensory impulses were the visceral afferents (S2, 3, 4) accompanying the parasympathetics.

#### DISCUSSION

In determining any aspect of human visceral pain man has distinct advantages as an experimental animal. The opportunity for the present study was ideally provided by a selected group from several hundred hypertensive patients subjected to sympathectomy for their disease. Since the extent of the operation was believed to interrupt all or the majority of sensory nerves thought to contribute to abdominal visceral sensation, it was not unexpected to find that bilateral sympathectomy from Th7 to L3 eliminated all pain sense from the abdominal viscera (exclusive of the pelvic viscera). The study provides comparatively little information concerning the segmental innervation of the viscera but once the basic fact is established that visceral analgesia can be produced the refinements can follow. There is much to suggest, for example, that the greater splanchnic nerve plays a major role in the sensory pathway since histologically it contains a large percentage of afferent fibers and any minimal stimulation of the nerve (traction, crushing, faradism) in the unanesthetized patient causes severe and diffuse pain. Yet the study shows further that additional sympathectomy is necessary to denervate the ureter.

The balloon distention studies of the stomach and intestine in the normal are comparable in their results to those set down in Jones'<sup>26</sup> admirable monograph. Our postoperative balloon studies show that unilateral sympathectomy affects sensation of only the homolateral side of the colon while both sides appear to innervate the stomach and small intestine. There is a slight discrepancy between the findings in the small bowel after unilateral sympathectomy and those reported by Bentley and Smithwick'<sup>27</sup>. The latter reported the elicited pain to be on the side of the midline away from the side of the

sympathectomy This discrepancy is not so important, however, since the direct stimulation of the small bowel through the open abdomen after unilateral sympathectomy showed some tendency to this contra-lateralization of the pain

Since the digestive tract is embryologically a midline structure it is not surprising that most of it appears to possess a bilateral sensory supply It is more remarkable that the right and left parts of the colon appear to have lost their dual supply The unusual finding of the apparent laterality of innervation of the lesser curvature of the stomach on intra-abdominal inspection is reported just as it was found, it may require additional study

The lower end of the colon, i.e., the rectum, may have visceral sensory supply but like the oral end of the digestive tract the chief sensory supply seems to be somatic White<sup>21</sup> has commented on similar findings of preservation of sensation in the lower colon following sympathectomy

The intra-abdominal tests indicate convincingly that the pain sensitivity of the stomach and bowel is related to the mesentery or the visceral mesenteric junction and not to the remainder of the bowel wall There has been conflict in the past on this point through the fact that Pacinian corpuscles exist almost wholly in the mesentery of the bowel had led many to doubt the existence of pain receptors except in the mesentery

The line of demarcation anatomically between parietal and visceral peritoneum is not always certain and it has in places been arbitrarily drawn The parietal peritoneum is usually presumed to be supplied by somatic afferents and this must be the case if one speaks of the ventral peritoneum because after bilateral sympathectomy this area possessed all its normal sensitivity But the dorsal peritoneum overlying the head of the pancreas, for example, is also referred to anatomically as "parietal" in spite of the fact that it possesses Pacinian corpuscles<sup>28</sup> and loses its pain sensitivity after bilateral sympathectomy

The appreciation of temperature in the stomach has been investigated by Wolf and Wolff<sup>7</sup> Working with a man who had possessed a gastric fistula for many years they found that water in a 10 cm bag in the stomach could be identified as hot and cold above or below 40° to 18° C, and beyond these extremes, variations of 3 degrees could be detected The subject described the sensation as an area the size of his fist deep in the epigastrium but when the balloon was placed near the lower end of the esophagus a more intense sensation was elicited which was felt in the substernal area Our observations tend to corroborate theirs and also to show that temperature sense (always closely allied with pain sense) is eliminated from the stomach by interruption of the sympathetics

Past studies on sensation of the extra-hepatic biliary tract<sup>29, 30, 31, 32, 33</sup>, as well as the present ones, show agreement in the area of constant reference of pain in the epigastrium The occurrence of associated pain in the back in some subjects appears to be dependent on stimulation of the ducts, possibly at the sphincter of Oddi The work of Davis, Pollock and Stone<sup>11</sup> shows that sensation in the gallbladder of dogs is supplied exclusively by the visceral

afferent nerves accompanying the sympathetics and more particularly the right splanchnic. Our studies in man show that the extra-hepatic ducts possess a bilateral sensory innervation although there were no observations on the results of distention of gallbladder after either right or left unilateral sympathectomy. Even though this item of information is lacking, it is fair to assume that in man the gallbladder too has a bilateral innervation and this assumes practical importance if nerve sections are to be put to use in the relief of pain.

The head of the pancreas has also been found in our studies to have a bilateral innervation. The importance of this finding was exemplified in a patient who had intractable pain from chronic calcareous pancreatitis of several years' standing. Her initial pain was in the mid-epigastrium and back. After right-sided resection of the splanchnics and ganglionated chain from the seventh thoracic to the third lumbar the former pain disappeared but pain of less degree now existed in the left hypochondrium. This left-sided pain was enhanced or duplicated by extra-abdominal pressure over any part of the palpable pancreas and in addition discretely localized stimulation (pressure and faradism) of the head of the pancreas after right sympathectomy caused left-sided pain. Following a left-sided sympathectomy all spontaneous pain ceased and no tenderness could be elicited on pressure over the previously tender gland (postoperative follow-up, 9 months).

The unilaterality of the sensory supply of the kidney and ureter from the evidence of these studies is definite and there is the additional suggestion that nerves other than the splanchnic play a role in sensory transmission at least for the ureter.

The investigations of Learmonth<sup>25</sup> led to his formulation of the triple sensory supply to the urinary bladder. Visceral afferents of the sympathetic system traverse the hypogastric nerves and plexus and the lumbar ganglionated chains. Visceral afferents of the parasympathetic system traverse the pelvic nerves which have their origins from the 2nd, 3rd and 4th sacral nerves. The somatic afferents traverse the pudendal nerves which originate from the 3rd and 4th sacral nerves. Our observations indicate that the interruption of any of the following nerve supply will not eliminate bladder sensation: bilateral lumbar sympathetics, parasympathetics, and pudendals (by section of all sacral nerve roots), bilateral lumbar sympathetics and both pudendal nerves. But interruption of all these will result in an insensitive bladder.

While the incentive to carry out these investigations was motivated primarily by a desire to learn something more about visceral sensation, some concern existed regarding the possible undesirable effects of the sympathectomies now being performed on so many patients with hypertensive cardiovascular disease. There is little doubt that after a bilateral thoracolumbar sympathectomy the visceral pain component of many abdominal diseases will be absent but in the most important ones (those, for example, that cause the acute surgical abdomen) there should always be other symptoms and signs. In two of our patients who had had bilateral thoracolumbar sympathectomy peptic ulcers perforated without there being any previous pain of the ulcer.



but the patients vomited and showed all the signs of acute peritonitis which led to early diagnosis and successful operation. So far none of the several hundred sympathectomized patients of our series is known to have developed acute appendicitis, cholecystitis, or any other abdominal surgical disease. However, it is now our practice to perform cholecystography on most patients who are to undergo sympathectomy for hypertension, if gallstones are discovered cholecystectomy is advised unless otherwise contraindicated.

### CONCLUSIONS

Studies of visceral sensation before and after sympathectomy in which the splanchnics and ganglionated chains are removed from Th7 to L3 on one or both sides show the following:

1 Pain sense in the stomach, intestine (except the rectum), extrahepatic biliary tract, pancreas, kidney, and ureter is mediated wholly by visceral afferent nerves which accompany sympathetic nerves within the area of the operative excision.

2 The kidney and ureter and the two sides of the colon have a homolateral sensory supply, but the remaining organs, with the possible exception of the gastric mesentery, have a bilateral supply.

3 Pain sensitivity exists not in the walls of the stomach and intestine but in the proximal mesenteries and at the mesenteric-visceral juncture.

4 Adequate stimuli for pain include, distention of hollow viscera, traction and faradic stimulation of stomach and intestinal mesenteries, manipulation, traction, faradic stimulation of the extrahepatic biliary tract, pancreas, kidney pedicle and ureter.

5 There is perception for extremes of temperature in the stomach, the afferent pathway accompanies the sympathetics.

6 The urinary bladder has a triple sensory supply via the visceral afferents of the sympathetic and sacral parasympathetic systems and the somatic pudendal nerves.

7 Interruption of appropriate sympathetic nerves may be employed for relief of intractable pain from some types of abdominal visceral disease.

8 The extensively sympathectomized patient due to the loss of visceral pain sense may undergo certain alterations in his response to visceral disease.

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DISCUSSION —DR LESTER R DRAGSTEDT, Chicago I should like to congratulate Drs Ray and Neill on this interesting and, I think, very important contribution Physiologists have felt for some time that the sense of hunger is due to contractions of the empty stomach

The sensation of hunger is apparently not abolished by complete section of the vagus nerves to the stomach. I should like to ask the authors if they have made any observations on the hunger sense in patients following extensive sympathectomy. I am interested in the report that sympathectomy produces complete relief of ulcer distress. This observation corroborates the work of the earlier French surgeons. We have observed a similar complete disappearance of the typical ulcer pain and distress following complete section of the vagus nerves to the stomach. Following this operation, however, the typical distress can be reproduced again by introducing 200 cc of 5 per cent hydrochloric acid into the stomach. I should be interested to know if the authors have performed such an acid test on patients with peptic ulcer who have undergone extensive sympathectomy.

DR FREDERICK L. REICHERT, San Francisco: Dr. Bronson Ray has talked about thoracolumbar sympathectomy. I am not sure if I know what he is talking about, is he referring to splanchnicectomy and thoracolumbar sympathectomy, or each alone? If he had done splanchnicectomy and made these observations it would be important. This should be made clear, otherwise things are mixed up. I am glad to hear Dr. Dragstedt say these patients had pain after vagotomy when hydrochloric acid was given.

DR WM. BABCLAY PARSONS, New York: Last year in the discussion of Dr. Whipple's paper on radical pancreatectomy for pancreaticolithiasis, Dr. Smithwick reported thoracolumbar sympathectomy in one case. I think the result reported by Dr. Ray is most interesting, but I believe it emphasizes the very important decision which must be made as to the type of therapy required in these cases. We recently had a young man of 22 with intractable pain and beginning morphine addiction due to pancreaticolithiasis in the head of the pancreas. A radical operation removing the head of the pancreas was done. He made an uneventful recovery from the operation. He has gained 30 pounds in weight and his condition is most satisfactory. I would like to question whether he is not better off now, having had the head of his pancreas removed with the duodenum, than he would be were he robbed of a considerable portion of his visceral sensation for the rest of his life.

DR LOYAL DAVIS, Chicago: Drs. Ray and Neill are to be congratulated on this very fine piece of physiologic work in visceral pain carried out upon the human. They have corroborated the work which was first done experimentally in our surgical laboratory and later extended in our studies upon visceral pain. Experimentally, we could stop all evidences of pain in the cat, produced by distention of the common duct and gall-bladder, when the right splanchnic nerve or the right thoracic sympathetic trunk were removed. It was very clear to me what Dr. Ray stated that they did in their experiments and the portions of the sympathetic system removed in their patients.

DR BRONSON S. RAY, New York (closing): It is our belief, Dr. Dragstedt, that following bilateral thoracolumbar sympathectomy, or even total sympathectomy, patients still have hunger sensation. I was also aware that the interruption of the vagi has no apparent effect on hunger and neither of them prevents nausea and vomiting. It has been my hope that we might have a suitable case for study in which both the sympathetic and vagus supplies to the stomach were interrupted. Until such a case is studied, it is impossible to draw final conclusions. With regard to the induction of gastric pain by the administration of acid, we have not employed that test in our sympathectomized patients but shall do so.

In answer to Dr. Reichert's criticism, I would repeat that this study of visceral sensation was made on a group of patients who had had unilateral or bilateral thoracolumbar sympathectomy for treatment of hypertension. In each case the ganglionated chain was removed from the seventh thoracic to the third lumbar, and the greater splanchnic nerve was resected between the celiac ganglion and a point above the contribution of the seventh ramus.

# THE ROLE OF PINEALOMAS IN THE CAUSATION OF DIABETES INSIPIDUS\*

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FROM THE DEPARTMENT OF NEUROSURGERY, THE LAHEY CLINIC, AND THE  
NEW ENGLAND BAPTIST AND NEW ENGLAND DEACONESS HOSPITALS

SINCE THE ORIGINAL INVESTIGATIONS on the antidiuretic effect of the secretion of the posterior lobe of the hypophysis by von den Velden<sup>1</sup> (1913), and the causation of polyuria following lesions of the hypothalamus by Camus and Roussy<sup>2</sup> (1913), the occurrence of diabetes insipidus in some patients with pituitary tumors or other lesions in the immediate suprasellar or chiasmal region was easily understood. On the other hand, the occasional report of marked polydipsia and polyuria in patients with tumors arising from the pineal body and apparently confined to this area which is so far removed from the supposed source of diabetes insipidus, was until recent years, incapable of explanation. In some reports of pineal tumors in patients having a high water intake and output a second tumor in the pituitary region was presumably the cause of the water imbalance (Horrax and Bailey,<sup>3</sup> 1925), but in other observations where no second lesion was found the diabetes insipidus was thought to be due to indirect pressure on the hypothalamus from internal hydrocephalus (Martin,<sup>4</sup> 1923).

As to the actual intracranial area responsible for polydipsia and polyuria, there were until very recently three theories, namely, that it was caused by a lesion of the posterior lobe of the pituitary gland, by injury to the hypothalamus, especially the tuber cinerea, or by interruption of a tract of demonstrated nerve fibers running from the hypothalamus through the pituitary stalk to the posterior lobe of the gland, the so-called supra-optico-hypophyseal tract. Fitcher<sup>5</sup> summarized the situation in 1931 as follows: "The tentative conception is that the nucleus supra-opticus is the centre that presides over the normal regulation of water balance. The fact that this centre is connected by a definite bundle of fibres with the posterior lobe, the extract of which has such a potent effect in relieving the polyuria of many cases of diabetes insipidus, seems to be of the greatest significance. The existence of this tractus supraoptico-hypophyseus renders it probable that diabetes insipidus may result from lesions anywhere along its course as suggested by Zadek."

This theory was confirmed some ten years later when, according to Jones,<sup>6</sup> the work of Fisher, Ingram, Ranson and their associates from 1935 to 1941 reconciled the previously opposing views. Jones states "It has been shown that there exists a hypothalamicohypophyseal system, with an included supraopticohypophyseal tract, which operates as a functional unit, and

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\* Read before the Meeting of the American Surgical Association, March 25-27, 1947, Hot Springs, Va

that injury to any part of this system causes diabetes insipidus. Since secretion of the antidiuretic principle by the pars nervosa (of the pituitary) is dependent on innervation through this tract, the supraopticohypophyseal tract is a functional unit, and injury anywhere along this tract may result in diabetes insipidus."

It was not until the publication of the important case report by Stringer<sup>7</sup> in 1934 that the role of pinealomas in the causation of polydipsia and polyuria was correctly explained. This author studied a patient coming to autopsy, and found in addition to a small pinealoma replacing the pineal body, a solitary implant confined to the tuber cinereum of the hypothalamus (Fig 1)



FIG 1—Pineal tumor implant in hypothalamus (just posterior to optic chiasm, C)  
(From Stringer, S W, Yale J Biol and Med)

Martin and Davis<sup>8</sup> (1941) studied eighteen cases of pineal tumor in the Cushing Tumor Registry and stated that diabetes insipidus was present in 8 of these patients. They found implantations or "seedings" of the pineal tumors in many cases involving the pituitary body, the walls and floor of the third ventricle and the periaqueductal gray matter, but from such widespread implantations no support could be given to any theory as to a localized area responsible for the disturbance in water balance.

In the article already mentioned by Horrax and Bailey<sup>3</sup> there were twelve histologically verified cases of pinealoma from Cushing's clinic. Three of these patients showed well-marked diabetes insipidus, but in two of them a second tumor of totally different microscopic type involving the hypothalamic region was unquestionably the source of the fluid imbalance. In the third case, only a tumor in the pineal region was assumed at the time to be present (Fig 2), but it is quite likely that if sections from the floor of the

third ventricle or of the pituitary stalk had been studied microscopically, invasion of these areas by pinealoma cells might have been disclosed as in Case 1 of the patients recorded here

The diagnosis of pinealoma or a tumor arising from the pineal body has been made in 17 instances in the writer's brain tumor series during the past 14 years



FIG 2—Pineal tumor with associated diabetes insipidus without gross involvement of hypothalamic region (From Horrax and Bailey, *Arch Neurol and Psychiat*, 1925 )

In 12 of the patients the tumor was verified histologically either at operation or at autopsy. In the other five patients histologic verification has not as yet been possible, but in these cases localizing neurological signs combined with the visible ventriculographic evidence of a tumor projecting into the posterior portion of the third ventricle from the pineal region has certified the diagnosis beyond any reasonable doubt.

Of the total 17 patients five have shown well-marked diabetes insipidus. Two of these patients have been in the group with histologically verified tumors, the lesion in the other three having been demonstrated by ventriculography. In one patient with histologic verification at autopsy the tumor from

the pineal region was shown to have extended through the floor of the third ventricle to involve the hypothalamus and pituitary body, thus explaining the presence of the polyuria. The other patient whose lesion was verified microscopically, had a so-called "ectopic" pinealoma in the area above the sella turcica without clinical or other evidence of a growth in the pineal region. The



FIG 3—Ventriculogram of Case 1, showing dilated lateral ventricles, large calcification in pineal region and curved shadow of tumor just anterior to calcification bulging into third ventricle

diabetes insipidus in this patient was, of course, easily explainable, as in other tumors situated in the neighborhood of the pituitary stalk and contiguous structures. The tumor was removed at operation and the patient's polyuria has been greatly benefited.

The three patients whose tumors were demonstrated by ventriculography have all had roentgen therapy directed at the pineal region. In one of these patients there has been a significant reduction of the fluid intake and output, and excellent control of the residual situation can be maintained by the use of extremely small amounts of pitressin powder snuffed up the nose. This improvement may be due to the fact that the area covered by the roentgen treatment included a portion of the anterior third ventricle and hypothalamic

region. The other two patients still show a rather marked polyuria but both have accustomed themselves to their difficulty. One of them has received further courses of roentgen therapy directed both toward his pineal and suprasellar areas with no appreciable change in his intake and output.

#### REPORT OF CASES<sup>\*</sup>

**Case 1**—*Partly calcified pinealoma in a child 12 years of age. Diabetes insipidus. Death following exploration of pineal region. Extension of tumor through floor of third ventricle into hypothysis.*

This child, P. P., was referred by Dr. Harvey Cushing and was admitted to the New England Deaconess Hospital on July 7, 1936. During the year previous to this the patient had been drinking large quantities of water and voiding similar large amounts of



FIG 4—Median sagittal section of brain in Case 1. Pineal tumor between posterior end of corpus callosum and corpora quadrigemina protruding into third ventricle. (This and Figs 5 and 7 to appear also in J. Neurosurg.)

urine. The 24-hour amounts measured at the New Haven Hospital ranged from 3,350 to 4,625 cc intake and 4,100 to 4,350 cc output. The specific gravity of urine was 1.008. One month prior to his admission to the Deaconess Hospital the child had developed symptoms of increased intracranial pressure. Neurological examination was negative. A ventriculogram on July 8, 1936, disclosed dilated ventricles, a large pineal calcification and

<sup>\*</sup> The records of four of the cases reported here have been utilized previously from other standpoints. An article incorporating Cases 1 and 2 has been accepted for publication by the Journal of Neurosurgery. Cases 3 and 4 were published as Cases 3 and 4 of the following article: Horrax, Gilbert and Daniels, J. T. The conservative treatment of pineal tumors. Surg. Clin. N. Amer., 22: 649-659, 1942.



the projection of a tumor mass into the posterior portion of the third ventricle (Fig 3) A transventricular operation on the same day was undertaken to try to remove the growth but this was unsuccessful and the patient died three days later

*Pathologic Studies* These were made by Dr Louise Eisenhardt, of the Cushing Tumor Registry, New Haven, to whom I am greatly indebted not only in this instance but also in Case 2

A median sagittal section of the formalin fixed brain showed the gross relationships of the tumor in the pineal region (Fig 4) This was microscopically a typical pinealoma (Fig 5)



FIG 5—Photomicrograph of pinealoma surrounding calcification (lower part of figure) in Case 1 ( $\times 150$ )

Because the patient was known to have had diabetes insipidus, Doctor Eisenhardt made sections of the floor of the third ventricle and of the hypophysis, and both were shown to be invaded by pinealoma cells, the invasion in the pituitary being confined to the posterior lobe (Fig 6)

*Discussion* Although the lesion causing polyuria in this patient was not quite as discrete as in Stinger's case where the pinealoma implant was confined to the tuber cinerea, nevertheless the invasion of the hypothalamic-hypophyseal tract was extremely localized and therefore highly significant as supporting clinically the experimental work referred to previously in the quotation from Jones

*Case 2—"Ectopic" pinealoma in the suprasellar region in a child of 12 Diabetes insipidus Operative removal of tumor followed by roentgen therapy Excellent clinical result with marked improvement in polyuria*

The patient, S F, was referred by Dr H Magendantz, of Boston, and admitted to the New England Deaconess Hospital on February 2, 1942 He had developed an excessive thirst and urinary output about two months prior to admission necessitating his

getting up three or four times at night to void. His 24-hour urinary output in the hospital was 3,140 cc, the specific gravity of the urine varied from 1.003 to 1.012.

Aside from general physical underdevelopment there were no significant neurologic findings, but roentgenograms of the skull showed a distinctly enlarged sella turcica with depression of the floor into the sphenoid sinus.

It was assumed that the child had a craniopharyngioma and on February 3, 1942, a right frontal craniotomy disclosed a solid tumor situated between the optic nerves. A very complete extirpation of the tumor was accomplished, and the child made an uneventful convalescence.



FIG 6—Pinealoma (at right) invading posterior lobe of pituitary (center) normal anterior lobe at left. Case 1 ( $\times 150$ )

Because the original pathologic report on the tumor had indicated that it was probably a malignant growth of testicular origin the patient received postoperatively 12,000 r units of roentgen therapy through several ports directed toward the suprasellar region. No evidence of a tumor in the genito-urinary system was disclosed clinically.

Sections of the tumor were subsequently sent to Doctor Eisenhardt and she established the diagnosis of ectopic pinealoma (Fig 7).

*Subsequent Course* This patient is alive and well, attending school regularly, five years and two months since his operation. He now drinks about 12 glasses of water a day compared to 17 to 20 glasses a day preoperatively. He voids only once at night compared to three or four times before operation.

*Discussion* The occurrence of diabetes insipidus in this case occasioned no surprise since the only evident clinical lesion was in the suprasellar region. The microscopic diagnosis of a pinealoma was, however, most unexpected. Whether the tumor is an isolated ectopic growth or whether it had its origin from a tumor in the pineal region which has never manifested itself clinically is obviously as yet undeterminable. It is likewise open to question whether

the operative removal of the tumor or whether the heavy course of roentgen therapy played the major role in the patient's recovery and in the subsidence of his diabetes insipidus

*Case 3—Pineal tumor demonstrated by ventriculogram in a young man of 20  
Diabetes insipidus Roentgen therapy Subjective improvement*

B N was referred by Dr Alexander Marble, of Boston, and was admitted to the New England Deaconess Hospital on May 28, 1939. He had been drinking excessive quantities of water and voiding similar amounts of urine for eight or nine months. He had likewise had severe headaches and "fainting" spells for a similar period.

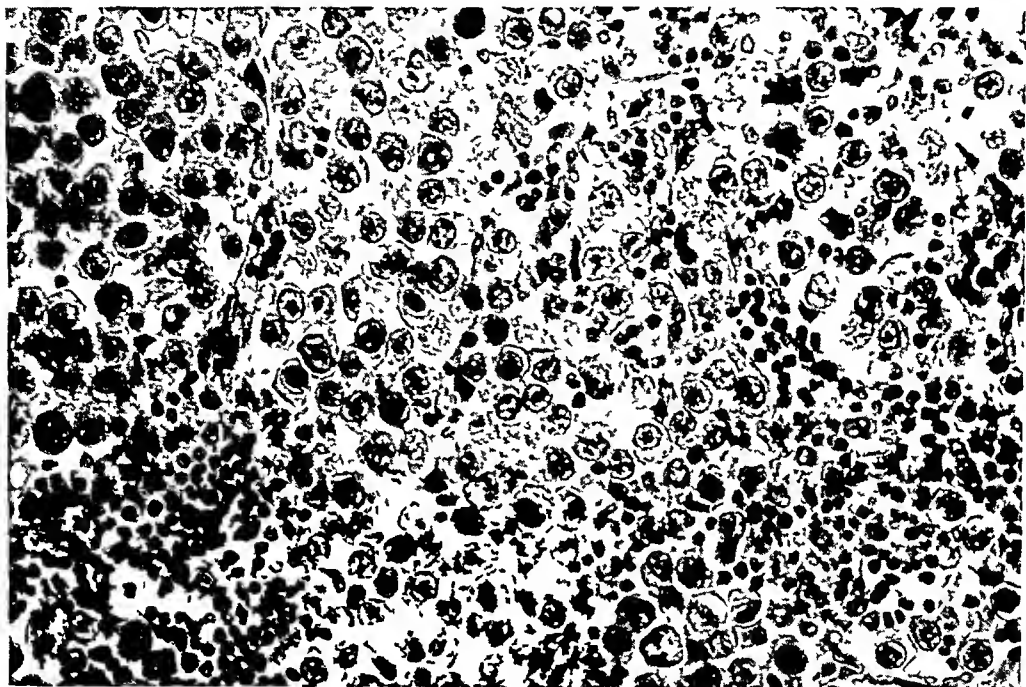


FIG 7—Typical pinealoma with large, pineal parenchyma cells and small lymphoid cells  
Case 2 (X 400)

His measured 24-hour fluid intake in the hospital varied from 4,600 cc to 6,450 cc and his output from 3,700 cc to 7,800 cc. The specific gravity of the urine varied from 1.003 to 1.014.

Neurologic examination disclosed limitation of conjugate movement of the eyeballs above the horizontal plane, his pupils were unequal, the right being larger than the left, and neither pupil reacted to light although they did react to accommodation.\* His fundi showed slight edema of the optic disks.

By the use of pituitary powder in the nose his fluid intake could be reduced temporarily to between 1,380 and 1,440 cc and his output to between 1,590 and 2,100 cc.

On June 26, 1939, a ventriculogram was made because of his intracranial symptoms and showed dilated lateral ventricles with a rounded mass protruding into the posterior portion of the third ventricle (Fig 8).

In view of the patient's relatively normal fundi no decompression was performed in this case, and between July 5 and August 3, 1939, he received ten roentgen treatments for a total of 1750 r units delivered through two ports. After the first treatment he became

\* These are the usual neurologic findings in patients having pineal tumors.

violently ill with nausea and vomiting so that the treatments had to be suspended temporarily. They were then resumed and by July 6 he showed distinct improvement in headaches. On July 22 the conjugate movement of his eyeballs upward was nearly normal. He was discharged on July 23, 1939.

*Discussion* This patient has been seen at intervals since he left the hospital and his general health had remained excellent when last seen August 16, 1946, seven years after his roentgen therapy. From the time of his discharge his



FIG 8—Ventriculogram of Case 3. Arrows point to rounded projection of presumed pineal tumor in posterior portion of third ventricle. Lateral ventricles somewhat dilated. (From Horrax and Daniels, Surg Clin N A, 1942.)

diabetes insipidus could be controlled with a smaller amount of pitresin or pituitary powder than before his roentgen treatments. He has, however, for the most part discontinued the use of these products and has accommodated himself to the excessive intake and output. At his last report in 1946 he stated that he was drinking and voiding about 10 quarts of fluid per day whereas four years previously he stated that these amounts were about 16 quarts.

*Case 4—Pineal tumor demonstrated by ventriculogram in a male of 24. Diabetes insipidus. Decompression and roentgen therapy. Marked improvement.*

C B was referred by Dr H N Kelly of Worcester, Massachusetts and was admitted to the New England Baptist Hospital on December 11, 1940. He complained of inordinate thirst and excessive urination over a period of seven weeks. He also had blurred vision and severe headaches. The patient stated that his fluid intake and output varied from 12 to 16 quarts per 24 hours. This could be reduced considerably by the use of pituitrin powder snuffed up the nose. The specific gravity of his urine varied from 1.003 to 1.005.

Neurologic examination showed early papilledema, pupils which reacted poorly to light, and impaired conjugate movement of the eyeballs above the horizontal plane

On December 13, 1940, a ventriculogram disclosed dilated lateral ventricles with a rounded shadow bulging into the posterior portion of the third ventricle from the pineal region (Fig 9) A right subtemporal decompression was carried out the same day

Between December 26, 1940, and January 6, 1941, when he was discharged, the patient received nine roentgen treatments directed at the pineal region, through three portals for a total of 2,700 r units He was considerably improved and relieved of all pressure symptoms on leaving the hospital



Fig 9—Ventriculogram of Case 4 Arrows indicate curved outline of presumed pineal tumor projecting into posterior portion of third ventricle Lateral ventricles dilated (From Horrax and Daniels as in Fig 8)

*Discussion* This patient has reported by letter and in person on many occasions since his operation and roentgen therapy His general health has remained excellent

His fluid intake and output has stabilized at six to eight quarts for the 24 hours In his own words, "To maintain this degree of water balance requires the smallest possible amount of powdered posterior pituitary that can be placed on the small end of a toothpick Between two to three hour intervals for these doses remains about constant" This letter was dated March 10, 1947

The patient reported in person on March 18, 1947 He was in excellent condition with an entirely negative neurologic examination

In respect to his diabetes insipidus he volunteered that he felt sure his excessive fluid intake had become somewhat of a habit with him since when water was not easily accessible the amount of his intake and output was cut down one third to one half for days at a time There is no doubt, therefore,

that he has had great relief from this condition as a result of his roentgen therapy

**Case 5**—*Pinealoma demonstrated by ventriculogram in a male of 31 Development of diabetes insipidus nine years after decompression and roentgen therapy*

R. M. was admitted to the Peter Bent Brigham Hospital on October 24, 1932, complaining of headaches, vomiting and blurring of vision of six weeks' duration. Neurological examination showed bilateral choked disks of 3 to 4 diopters. His pupils were unequal and reacted sluggishly to light and accommodation.



FIG. 10.—Ventriculogram of Case 5. Large tumor shadow (arrows) presumed pinealoma, bulging into posterior portion of third ventricle. Lateral ventricles dilated. (Kindness of Dr. M. C. Sosman.)

A ventriculogram October 26, 1932, showed marked dilatation of the lateral ventricles with a convex projection into the posterior portion of the third ventricle from the pineal region (Fig. 10). On October 28, 1932, a right craniotomy with decompression was carried out by the writer, the idea at that time being to allow the ventricle to expand still further in order subsequently to do a transventricular approach to the pineal tumor. This fortunately has never been necessary.

Following his operation the patient was given five series of roentgen treatments from November 1932 to March 1934 by Dr. M. Sosman, who has kindly supplied the dosage and has allowed me to obtain a print of the ventriculogram. Each series consisted of four treatments of 750 r units to either side of the head, directed toward the pineal region,

a total of 1,500 r units per series. The patient was discharged November 14, 1932, with all symptoms relieved.

He remained well for nine years until December 1941 when he developed a severe diabetes insipidus which was helped to some extent by injections of pitressin in oil. Between January 7, 1942 and March 17, 1942 he was given further roentgen therapy, 1,000 r units were delivered to the suprasellar region and the same amount to the pineal area. However, his intake and output has averaged 3,500 cc each per 24 hours and it is necessary for him to attach a urinal at night. The specific gravity of the urine varied from 1.002 to 1.010.

He reported in person on March 24, 1944. His fundi were normal except for slight secondary atrophy, his pupils were equal and reacted well to accommodation and fairly well to light. His ocular movements were normal and his decompression was flat. He reported again on June 15, 1944 after a trial of pitressin powder snuffed up the nose but this had not influenced his polyuria. He was then given a second series of roentgen treatments, 600 r units being delivered to three ports for a total dosage of 1,800 r, directed toward the suprasellar region.

A letter from the patient on March 10, 1947 states that his measured intake and output per 24 hours is still approximately 3,500 cc for each.

*Discussion* Aside from the long useful survival (14 years) following decompression and roentgen therapy for a patient with neurologic and ventriculographic evidence of pineal tumor, the development of diabetes insipidus nine years after his original intracranial pressure symptoms is interesting. He like the others in whom the water intake and output is troublesome, is nevertheless at his usual work and has accommodated himself to the handicap very well.

#### SUMMARY

Diabetes insipidus has been present in two patients with histologically verified pineal tumors and in three other patients in whom such a tumor has been demonstrated beyond reasonable doubt by neurologic and ventriculographic evidence. In one patient (Case 1) the tumor cells were shown microscopically to have invaded the hypothalamus and posterior lobe of the pituitary body, thus involving the tract of nerve fibers, interruption of which has been shown to be responsible for diabetes insipidus. In Case 2, the growth was an ectopic pinealoma in the suprasellar region obviously compressing the area in question and when this tumor was removed operatively the polyuria was greatly lessened.

In the three patients whose tumors have been depicted by air studies a similar invasion of this tract, as in Case 1, seems probable. These three patients have received roentgen treatment in two of whom the rays were directed not only at the pineal region but also to the suprasellar area which included the hypothalamic region as well. Their general condition has remained excellent for six and one-half to 14 years following roentgen therapy. The diabetes insipidus has been considerably relieved in one and probably in two of these patients. It is possible that the water imbalance may persist because partial interruption of the nerve tract from hypothalamus to pituitary is permanent even though the tumor cells originally causing this interruption have been destroyed by the roentgen rays.

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DISCUSSION—DR PETER HEINBECKER, St Louis The interrelationships of the hypothalamus and the hypophysis are so complex that it is not possible always to interpret them from clinical material We must have recourse to the experimental laboratory for knowledge necessary to understand the mechanism of diabetes insipidus associated with tumors in the region of the pineal and in the region of the hypothalamus itself Experimental work to determine the essential lesion in diabetes insipidus has been in progress in our laboratory for years As a result of these studies, the following conclusions are permissible

1 Experimental diabetes insipidus in dogs follows destruction or denervation of the entire neurohypophysis, all the cells of paired supraoptic nuclei and the rostral half to one-third of the paired paraventricular nuclei innervate the neurohypophysis

2 The presence of pars distalis is not essential to a marked diabetes insipidus lasting many months, but is essential to its permanent maximum maintenance through trophic effects on thyroid and adrenal cortex

3 Moderate diabetes insipidus may exist in the presence of the pars distalis when the residuum of functional neurohypophysis is sufficient to prevent any increase in urine output in the absence of the pars distalis

4 When sufficient exogenous thyroid and desoxycorticosterone are administered simultaneously to produce a marked increase in urine output of the totally hypophysectomized diabetes insipidus dog, the additional administration of anterior lobe extract decreases the urine output

5 Thyroidectomy immediately terminates the transitory polyuria of simple hypophysectomy It will not eliminate but may depress somewhat the polyuria of the totally hypophysectomized dog (complete absence of all divisions of the hypophysis)

It has been shown that in the dog the denervation of the neural hypophysis results in a loss of basophil cells in the glandular hypophysis leaving only eosinophil and chromophobe cells A lesion in the posterior hypothalamus so placed as to sever fibers rostral to the paired paraventricular nucleus, from the thalamus and subthalamus, results in a considerable decrease in number of hypophyseal basophil cells and in the density of granulation of those remaining In such dogs obesity develops, but not diabetes insipidus

The eosinophil cells have been shown by us to be trophic to the adrenal glands, to the corpus luteum, to the androgenic cells and to the renal tubule cells Their overaction can account for many of the signs and symptoms associated with Cushing's syndrome



and with lesions in the region of the pineal gland. Evidence for an endocrine function of the pineal has not been established.

As a result of these observations, we can account for the obesity associated with pinealomas as being due to the exaggerated action of the eosinophil cell and adrenal cortical hormones. We can account for excess growth and sex changes because the eosinophils secrete the growth and the androgenic hormones.

DR BYRON STOOKRY, New York. Dr Horrax is to be congratulated on presenting an interesting clinical problem. He calls attention to the fact that pinealomas may extend into the third ventricle and forward so as to involve the hypothalamic region, where they can produce diabetes insipidus. These tumors are occasionally extremely soft and may extend even into the fourth ventricle and forward to surround the optic chiasm, as was illustrated by a patient whom I had operated upon some five years ago, the patient doing well until recently when he began to show signs of bitemporal hemianopsia. This clinical sign was difficult to explain on the basis of a posteriorly placed pineal neoplasm. At autopsy it was found that the tumor had extended forward so as to implicate the optic chiasm. I remember a similar patient of Dr Tilney's in which the tumor had extended not only forward along the base but also posteriorly into the posterior fossa. The growth was soft and extensive in character. Thus, these tumors may be discrete tumors and calcified or if they take on more rapid growth, may by extension invade the anterior cranial fossa as well as the posterior cranial fossa.

Dr Horrax was too modest to refer to his earlier work, of which he was among the first to describe the ocular signs associated with pinealomas, which are almost diagnostic of them.

DR JOHN MARTIN, Chicago. In 1939 I had the opportunity to review, with Dr Louise Eisenhart, the case histories of 18 patients with pineal tumor in the Cushing files. Many of these are familiar to Dr Horrax. Among these, eight patients had diabetes insipidus, but these eight patients had not been studied specifically for any implantations of tumor in the hypophyseal region and, in some cases, destruction of the third ventricle was so great it would have been difficult to determine the exact cause of the diabetes. At the same time we were running experiments in our laboratory on dogs, cats, rats and monkeys to determine the effect of the destruction of the pineal gland in immature animals. Destruction of the pineal gland was carried out by means of the Horsley-Clark stereotaxic apparatus which gave a discrete lesion without damage to any of the surrounding structures. While we found evidence of change in our animals in both somatic and sexual development we did not have any instance of diabetes insipidus in our entire series. Neither did we find any destruction of the neural pathways leading from the pineal gland and region thereof or any other changes in the third ventricle or brain stem. We did note an increase in the eosinophilic cells in the male animals. Dr Horrax's studies are in keeping with the work done earlier in our laboratory when the paraventricular nuclei were destroyed by electrolytic lesions in cats, following which the pancreas was totally removed. Such animals did not develop diabetes.

DR FRANCIS C. GRANT, Philadelphia. Dr Horrax has outlined the situation with regard to the treatment of tumors in the pineal recess and the posterior part of the third ventricle in his usual thorough manner. It is certain that many of the tumors in this area respond readily and in a definitive fashion to x-ray treatment. It is my experience that they are very difficult to handle from an operative standpoint. If these tumors can be attacked by any method short of direct surgery, it is a great advantage insofar as the patient is concerned. In the past ten years we have had 13 cases in which the tumor was located in the posterior part of the third ventricle. In this group there have been seven deaths resulting directly from operative intervention. In three cases both an attempt at surgical removal and subsequent x-ray treatment were ineffective and the

patient succumbed within a year. Three cases have survived ten, seven, and six years. In two cases, surviving for ten and seven years, operative removal was obviously incomplete. X-ray therapy was instituted. In these cases, partially calcified prior to attempted extirpation and x-ray therapy, not only has the patient remained symptom-free but the calcification within the walls of the tumor has definitely increased. In the third case, presenting a minimal calcification preoperatively, all the calcified area, at least, was removed during the surgical attack, although the operative note states that the extirpation of the tumor is probably incomplete. In this case the patient has remained well and subsequent intensive x-ray treatment has produced no further calcification. In each of these three surviving cases and in the three cases that were attacked surgically, but who did not survive the operative procedure and x-ray therapy for more than a year, a large decompression was always afforded at the base of the bone flap. A decompression in these cases is valuable, in our opinion, for two reasons. Primarily, it helps carry the patient through his early postoperative course when edema is sure to follow the operative trauma. Secondly, it permits expansion of the ventricle locally so that, if a secondary attack on the tumor seems indicated, an enlarged ventricle will be found and the approach to the tumor through the ventricle may be made with greater ease. I have a very definite impression that, in these tumors in the pineal recess and the posterior part of the third ventricle, decompression, plus x-ray therapy, will in the long run, possibly, show more satisfactory results than a direct attempt surgically to remove these deeply seated and inaccessible lesions.

DR HOWARD C. NAFFZIGER, San Francisco. It has been our experience also that a considerable percentage of pineal tumors are responsive to x-ray therapy. The immediate danger, as stated, is from reactionary swelling of the tumor with complete obstruction of the aqueduct, and the consequent dangers of intracranial pressure. It seems, however, that the precautionary subtemporal decompression recommended by Dr. Horrax should not pass without comment. It does not relieve the obstruction, and will not do more than provide a very temporary and probably inadequate relief for fluctuations in the amount of intraventricular fluid. As a protection, it seems logical and I believe it is advisable to provide for ventricular puncture or temporary continued drainage of the fluid extracranially until the danger is past.

DR GILBERT HORRAX, Boston (closing). I want to thank all the discussors very heartily. In regard to Dr. Martin's comment, I am familiar with the work he and Dr. Davis did in connection with the Brain Tumor Registry. I did not mention it, but it appears in the bibliography of the paper. So far as Dr. Giant's discussion is concerned, I did not mean to imply that every tumor in the posterior portion of the third ventricle would respond to this treatment. Some tumors, however, do respond, and we thought some less severe measure than exploration should be done to see if this would be so.

The question Dr. Naffziger brings up is a very interesting one. I realize that what he says is theoretically true. You cannot expect permanent relief from subtemporal decompression in lesions which block the aqueduct. I can recall, however, in the old days before ventriculography was available, when we were dealing with unlocalized tumors, we would do a subtemporal decompression. The patients would be improved sometimes, even though later it turned out to be a subtentorial tumor which blocked the aqueduct. The two patients who had decompression and went through x-ray treatment did very well. In the third, we did not do a decompression and he had a severe upset during the course of treatment, doubtless due to blocking of the aqueduct of Sylvius. Just what decompression does we do not know, but apparently it lets fluid get through temporarily at least, so patients do not have upsets during treatment. So far as the catheter is concerned, that is left in for a matter of only 24 or 48 hours at most, attached to a sterile bag. That is done in all our cases now, but it was not in during the time of x-ray treatment.

# THE TREATMENT OF FOCAL EPILEPSY BY CORTICAL EXCISION\*

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FOCAL EPILEPTIC DISCHARGE can now be localized in all areas of the cerebral cortex. Excision of partially damaged convolutions adjacent to meningocerebral scars or in areas of brain atrophy has proved to be effective treatment. This is demonstrated in the series of cases about to be reported. Attention will be focused upon surgical technic and the elements in these cases that seem to promise success or failure.

## A LITERATURE

Attempts to stop epileptic seizures by making a hole in the skull doubtless began in the era of prehistoric trepanation. Surgeons began to carry out craniotomies for this purpose in the early nineteenth century with no other therapeutic plan than to open and look. Nevertheless, the published reports of this period are surprisingly optimistic†. Once antisepsis and asepsis had opened the flood gates of surgery, there appeared extravagant claims of "cures" of epilepsy by many types of operation, from craniotomy to sympathectomy and resection of the large bowel. However, in the face of critical analysis, this optimistic phase passed and today, except for the removal of brain tumors, the role of surgery in the treatment of the epilepsies has become small indeed in most clinics.

Sir Victor Horsley was the pioneer in the application of physiologic principles to the problem, and it is interesting that his first three craniotomies (1886) were undertaken for the cure of focal epilepsy. One patient had a meningocerebral scar, one a tuberculoma, and the third a post-traumatic cyst. Two years later, Keen (see Ballance, 1922) published three somewhat similar cases. However, eventual surgical opinion of the results of such a procedure is well expressed by a Philadelphia surgeon, Nancrede. After reporting success in 1888 and 1892 he wrote (1896) in a sadder and wiser vein that surgical excision could be considered no more than a palliative procedure because the surgeon left behind him a new scar in the place of the original lesion.

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† For example, see Wells (1812), Dudley (1828), Baron Larrey (1829), Heyman (1831), Astley Cooper (1839). Billings (1861) collected 62 reports of which 42 were called "cures".

Gerster and Sachs (1892), also Horne (1894), cast the same gloom upon this form of surgical therapy. Hadra (1894) emphasized the desirability of reproducing the patient's own seizure by electrical stimulation as well as the motor responses. Woolsey (1896) used an osteoplastic bone flap in his excision of the lesion in six cases, but had only one "cure." Kiause (1912) reported that he had carried out cortical excisions in 54 patients, of whom he considered four cured, but his follow-up was quite inadequate. He did state that the Kocher "valve" or decompression operation gave inadequate results in 34 cases.

Cushing (1908) reported 59 cases of epilepsy treated surgically, but he carried out "extirpation" in only 13 and included examples of brain tumor together with birth trauma and head trauma, so that it is not possible to estimate the elements responsible for the fact that 12 patients seem to have been made seizure free.

Excisions of localized areas of brain have been reported more recently in relatively small groups of cases by Little (1922), Foerster and Penfield (1930), Rowe and Watts (1936), Furlow (1938), German (1939), Voris (1943), with a varying incidence of "cures" and near-cures.

Penfield and Erickson (1941) published a complete analysis of all patients who had cortical excision carried out during a ten year period, 1929-1939. There were 115 patients who were thus followed from one to 11 years, with the result that 43 per cent were seizure free or had had one or two attacks, 26 per cent considered themselves 50 per cent improved, 9 per cent were slightly helped, and 22 per cent not improved.

#### B PATHOLOGIC NOTE

A variety of lesions may give rise to cerebral seizures, but there is no reason to call the patients epileptics in the common understanding of the term nor to suggest taint of inheritance. A brief reference may be made to the pathology of certain epileptogenic lesions\*. Brain lesions of many types are apt to produce some local destruction of nerve cells. After such destruction, neuronal regeneration does not occur in the central nervous system. But, unless all circulation to the part is destroyed, the neuroglia react in a positive way, producing gliosis. Destructive processes are also associated with phagocytosis of myelin and other material. The end result of these changes is gross atrophy of the involved convolutions.

*Meningocerebral cicatrix* When trauma or infection has involved a local area of the brain, there results an intermingling of connective tissue and neuroglial tissue which eventually produces a contracting scar. A connection is thus established between the cerebral vessels and the extracerebral vascular tree through the scar. Ganglion cells disappear at the center of the damaged area and at the periphery they are subjected to abnormal conditions.

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\* For further discussions see—Penfield (1927), Penfield and Humphreys (1940), Evans and McEachern (1937), Penfield and Erickson (1941), chapter IX.

*Local cortical atrophy* Compression and ischemia are capable of producing atrophy within the convolutions of the brain without the entrance of connective tissue into the scar, but with the appearance of a local glial overgrowth and the disappearance of ganglion cells in the zone of greatest involvement

*Local microgyria* At the time of birth it seems likely that the following sequence of events occurs. One, or a group of, gyri may be injured and partly destroyed by ischemia or by local compression during the period of the passage of the head through the birth canal. During the subsequent year of life, the normal portions of the brain grow very rapidly, each gyrus crowding outward and pushing the skull before it. The injured gyri do not grow, but are crowded in together. The important thing, however, is that they do not disappear. The total number of ganglion cells is greatly reduced within them, and the remaining cells are subjected to abnormal influences.

*Expanding lesions* Brain tumor or cerebral abscess as it expands destroys the ganglion cells and white matter. At the periphery of such lesions is found a zone in which the ganglion cells of the gray matter are able to survive but are subjected to abnormal influences similar to those about other lesions, that is, the blood supply to these ganglion cells is reduced to a critical level.

*Cysts and other abnormalities* may be the result of a congenital defect or of vascular occlusion. Complete interruption of circulation in a region results in a cyst. But at the periphery there may be found partially normal ganglion cells in atrophic gyri. If, on the other hand, the interference with circulation is only partial, only an area in which the gyri are atrophic results without central cyst formation.

This brings us to a realization of the fact that all of these factors which may produce epileptic seizures have a common feature, which is illustrated in Figure 1. This feature is the presence of a zone or area of ganglion cells, the circulation of which has been interfered with to such an extent that its continued life is threatened. It is at some point in these peripheral or partially destroyed zones that the actual focus is to be found, the focus in which the epileptic discharge originates. Histologic study of such areas indicates that there is a continuing variation in circulation which results in occasional, spotty destruction of ganglion cells even years after the original injury or compression.

Thus, it may be assumed that partial anoxemia, if not sufficient to destroy, produces in ganglion cells an abnormal state, a supernormal state in which spontaneous neuronal activity is increased. This increase may be called the *epileptogenic factor*.

It seems obvious that no neuronal discharge can originate in a cyst or tumor or scar that is devoid of nerve cells. It also seems obvious that if surgical therapy is to be effective it is not sufficient to cut adhesions or to open a cyst, or in some cases to remove a tumor. The epileptogenic focus in the marginal partly-involved gyri must also be removed, and, furthermore, it seems obvious that in this removal any gyrus that is involved should, where feasible,

be excised wholly, leaving the neighboring gyrus covered with its own blanket of pial blood vessels

### C ANALYSIS OF RESULTS

The patients included in this review of the results of radical surgical therapy of atrophic epileptogenic lesions of the brain were operated upon in the six year period 1939-44. Because this was the war period, when urgent problems took priority, many such patients were sent away without operation. The time of follow-up varies from one to seven years. All operations were carried out, or supervised by W. P., the follow-up analysis was made by H. S.

A total of 76 patients was operated on for epilepsy. Every one of the 76 has been followed up to the time of writing. Six of these had a second operation for further removal of epileptogenic tissue, making a grand total of 82 operations. There were 50 males and 26 females. Only one patient died as a result of the operation, his death being caused by an infected extradural hematoma and meningitis. The case mortality was thus 1.3 per cent, and the operative mortality was 1.2 per cent. Of the 75 cases to be followed, cortical excision was performed in 59 and craniotomy without excision in 16.

The results were determined as follows: a seizure must involve movement before it was counted as such, auras, without subsequent movement or loss of consciousness, were not counted as a seizure in the statistical analysis. All results were counted from the time the patient was discharged from the hospital.

The grouping<sup>\*</sup> of results is as follows: 0 = failure, 1 = 25 per cent improvement, 2 = 50 per cent improvement, 3 = 75 per cent improvement, 4 = 100 per cent improvement. The patient was asked in each instance to express his own conclusions in these percentages. Many who had gone for years with one, two or three seizures considered themselves completely cured, but such individuals were placed in Group 3. Those in Group 4 have had no attacks since leaving hospital.

Expressed in another way, Groups 4 and 3 are satisfactory. The result was a success. Group 2 includes the fair results and 1 and 0 are poor. Routinely, no medication was given following operation except phenobarbital, and that usually for a year or two in decreasing amounts. All patients had had thorough, prolonged treatment by various medications before resort to operation.

Of the 59 patients (Table I) who had a cortical excision, there were 15, or 25.3 per cent, who were completely free of seizures. The number and length of time they have been free is: 7 years—1, 6 years—2, 5 years—3, 4 years—2, 3 years—2, 2 years—3, and 1 year—2. Eighteen, or 30.5 per cent, were almost completely free and were placed in Group 3. Thus, a total

<sup>\*</sup> This method is borrowed from the system employed by the Presbyterian Hospital, New York, where the follow-up system has reached a high degree of efficiency under the direction of Professors Allen Whipple and Walter Palmer.

of 33 patients, or 55.8 per cent of the total, were free of attacks or had had only one or two, and considered themselves 100 per cent cured or almost so. Eight, or 13.6 per cent, were in Group 2. Adding Groups 2, 3 and 4 together, we find that there were 41, or 69.4 per cent, who had sufficient relief to make the procedure well worth-while. Seven patients, or 12 per cent, were only slightly improved, Group 1, while 11 more, or 18.6 per cent, felt that they derived no benefit from the operation and were therefore put in Group 0.

1 *Meningocerebral Scar Compared with Atrophic Cerebral Lesion* The nature of the simple cerebral lesion varied. Sometimes it consisted in simple

TABLE I  
RESULT OF OPERATION

Operation	Groups					Total Cases
	4	3	2	1	0	
Cortical excision	15	18	8	7	11	59
	25 3%	30 5%	13 6%	12%	18 6%	
	55 8%					
Craniotomy without excision	0	0	5	2	9	16
			32%	14%	54%	

convolutional atrophy. Occasionally there was little gross evidence of abnormality. There were 31 meningocerebral cicatrices and 28 cerebral lesions which were excised. In the former group there were nine patients, or 29 per cent, who were completely free as against six, or 21 per cent, with cerebral lesions. However in Group 3, nine patients, or 29 per cent, with meningocerebral cicatrix were "almost cured," while nine patients, or 32 per cent, were in the same group of cerebral lesions. If Groups 3 and 4 are combined, then 58 per cent of the meningocerebral cicatrices had a satisfactory result as against 53 per cent of the cerebral lesions, giving a slightly higher score of 5 per cent for the former.

2 *First Seizure After Operation* What are the chances of having a satisfactory result from operation if a seizure occurs within a few months of discharge from the hospital?

In the group of 16 craniotomies without excision (Table I), 14, or 86 per cent, began to have attacks in the first six months, while the remaining two had return of seizures in the second six months. In the cases where craniotomy was associated with excision, 18, or 30.6 per cent, had poor results (Groups 1 and 0). All of these patients had a speedy return of attacks within the first six months.

In Group 2, the first seizure occurred as follows: during the first six months after operation—4 patients, or 50 per cent, 7 to 12 months—1, 13 to 24 months—2, and 25 to 60 months—1.

In Group 3, the first or the only attack occurred as follows during the first six months after operation—5, or 28 per cent, 7 to 12 months—5, or 28 per cent, 13 to 24 months—7, or 39 per cent, 25 to 60 months—1, or 5 per cent

3 *Results According to Cause of Lesion* The initial cause of the lesion responsible for the attacks in each case was studied before and during operation. In many this was quite clear, but in some it was indefinite. If the cause was obscure, it was labelled "unknown."

TABLE II  
PROBABLE CAUSE OF CEREBRAL LESIONS

	Birth Injury	Head Injury	Infection	Unknown	Total
Cortical excision	17 29%	26 44%	9 15%	7 12%	59
Exploration only	3 19%	3 19%	0 0	10 62%	16

TABLE III  
RELATIONSHIP OF SURGICAL THERAPY TO CAUSE  
Groups

Cause	4	3 (4+3)	2	1	0	Total Cases
Birth injury	7 41%	6 35% (76%)	1 6%	1 6%	2 12%	17
Head injury	5 19%	8 32% (51%)	4 15%	4 15%	5 19%	26
Infectious process	1 11%	4 45% (56%)	2 22%	1 11%	1 11%	9
Unknown	2 29%	0 0 (29%)	1 14%	1 14%	3 43%	7

Injuries that obviously dated back to birth comprised 29 per cent of the excision group, as shown in Table II. Of these, 16 per cent (Table III) had a satisfactory result, with 41 per cent in Group 4 and 35 in Group 3. Gross head trauma accounted for 44 per cent of the excision cases (Table II), and of these 51 per cent had a good result (Table III). Infectious processes, such as healed brain abscess, meningitis and cortical thrombophlebitis, comprised 15 per cent, and 56 per cent of these had a satisfactory outcome. In only 12 per cent of the patients was the initial cause unknown, of these 29 per cent had a satisfactory result.

4 *Interval Between Brain Injury and Onset of Seizures* The histories of all 75 patients were studied to determine the length of time between production of the lesion and onset of the seizures. The analysis yielded the following figures:

**Birth injury**—None had an onset of seizures in the first year, while 18 per cent started having them in the two to five year interval. Thirty-five per



cent began in six to ten years, and 47 per cent in 11 to 20 years. Thus, 82 per cent had their first seizure after the age of five years.

**Head injury**—If the injury was due to head trauma after birth, 38 per cent began to have seizures in the first year after the accident, 50 per cent in the two to five year interval, 8 per cent—six to ten years, and 4 per cent—11 to 20 years. Thus, 88 per cent of these patients had onset of attacks within the first five years.

**Infection**—Only nine patients could have the cause of epilepsy traced to an infectious process, such as brain abscess, meningitis and cortical thrombophlebitis. However, 56 per cent of them had an attack within the first year and 22 per cent in each of the two to five and six to ten year intervals. Thus 78 per cent began having seizures within the first five years.

To summarize this portion of the analysis—Cause was assigned in 52 per cent of the 75 cases. The attacks began within the first year after the brain damage in 31 per cent of the cases. They began during the next four years in 33 per cent, and in the subsequent 15 years in 36 per cent of the cases. The longest free interval before onset of seizures tends to occur in the cases of birth injury.

5 *Relationship of Duration of Seizures to Outcome of Operation* In Table IV, the patients were grouped according to the period of time of operation after the onset of the attacks. Reference to the table indicates that the duration of the seizures has little or no effect upon the outcome of treatment by excision. It indicates also that the establishment of so-called "epileptic habit" is of no importance if the proper excision is carried out.

6 *Relationship of Aura to Result of Excision* The patient's aura or warning that an attack is imminent is the most valuable single localizing sign. The 59 patients in whom an excision was done were grouped according to their various auras to see if any prognostic indications could be discovered.

**No aura** Nineteen patients had no aura at all—either they lost consciousness at the outset or movement began without previous warning. Ten of these, or 53 per cent, had a good result following operation.

**Somatosensory aura** Twenty-four patients had a sensation in some part of the body before convulsive movements began, this sensation was variously described as numbness, tingling, pain, pressure or fullness. Fifty-four per cent had a successful result.

**Viscerosensory aura** Five patients had a visceral warning. Two of these had an epigastric sensation which ascended to the chin before consciousness was lost. One had a feeling of nausea, one epigastric pain, and one a unilateral body aura. Four of the five have had a satisfactory relief from seizures.

**Visual aura** Six patients were warned of an attack by visual sensations of lights or spots before their eyes. Half of them had a satisfactory operative result.

**Dreamy state aura** Two had an illusion of perception or an hallucination in advance of convulsive movements One had a good result

**Auditory-vertiginous aura** One patient had an aura of dizziness and buzzing, she was not helped

**Forced thinking** Two patients had an aura of thoughts which came to them and which they could not suppress Both of them have had good results

*7 Relationship of Site of Excision to Result* The cerebral excisions were grouped according to the area in which the excision was made, to determine what difference in outcome there might be Of course, many of the removals involved more than one lobe and in these the site of the major removal was taken as the group into which it fell The number of patients and the percentages of satisfactory results are as follows frontal pole—14 cases, 71 per cent satisfactory, midline frontal lobe—three, 0 per cent, central region—16, 69 per cent, temporal lobe—14, 50 per cent, parietal lobe—five, 40 per cent, occipital lobe—seven, 43 per cent The differences are not very significant, but the frontal pole and the central areas have a higher scoring

*8 Relationship of Pneumoencephalogram to Result of Excision* Pneumoencephalograms were made in 54 of the 59 patients In 78 per cent of these there was some degree of localized ventricular deformity which suggested an atrophic lesion Of those with such a deformity, 58 per cent had a satisfactory result Of the 22 per cent whose pneumoencephalogram was of no localizing value, only 42 per cent had a satisfactory result

An encephalogram was made in 15 of the 16 patients who had no cortical excision carried out Eleven, or 73 per cent, of these showed local atrophy, none of the patients were listed in the success groups

*9 Physical and Neurologic Examination* In 41 per cent of the patients, the physical and neurologic examination, exclusive of local injury or deformity of the skull, pointed to a local lesion Of this group, 67 per cent were in Groups 3 or 4 Of the 59 per cent whose examination did not localize a lesion, 49 per cent had a good result from operation

*10 Preoperative Electroencephalography* All of the patients had a preoperative electroencephalogram taken The method of recording has been described by Jasper elsewhere (see pp 380 to 455 in Penfield and Erickson, 1941) The preoperative electroencephalogram of each patient was classified in the manner described by Jasper and Penfield (1943)

The preoperative electrographic conclusions are tabulated in Table V for the 16 cases in which no excision was made at craniotomy and also for the 59 cases with excision This table does not include electrocorticography\* after exposure of the brain It may be pointed out that a superficial cortical focus is apt to give rise to potential changes of brief duration and high voltage that are recorded in the electroencephalogram as "spikes" A similar focus somewhat deeper, *i e*, in the gray matter at the bottom of a fissure or on the under surface of a lobe, appears in the scalp electrogram as a somewhat slower

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\* An estimate of the value of this procedure will be made in a subsequent report

alteration in potential called a "sharp wave" The delta waves referred to in Table V indicate brain injury either due to an advancing process or as the temporary result of severe seizures

When clinical studies indicate that there is a localized focus giving rise to periodic seizures, the electroencephalogram may be carried out repeatedly and hyperventilation, hydration or metrazol used to increase the activity of the focus until the source is mapped out Some sort of electrographic localization was thus worked out in all but three cases, and in two cases the electroencephalographic abnormality was unclassified In none of these cases was the result satisfactory

TABLE IV

RELATIONSHIP OF SURGICAL THERAPY TO PREOPERATIVE DURATION OF SEIZURES

Years Before Operation	Total Patients	Success Groups 3+4
1	3 - 5%	1 - 33%
2-5	25 - 43%	14 - 56%
6-10	16 - 27%	10 - 62%
11-20	9 - 15%	5 - 55%
21-30	6 - 10%	3 - 50%
	59	33 - 56%

TABLE V

PREOPERATIVE ELECTROENCEPHALOGRAMS

E E G	Negative Explora- tions	Success Groups 3+4	Exci- sions	Success Groups 3+4
Spike and/or sharp wave focus	4	0	21	11 - 52%
Same with contralateral transmission	5	0	16	14 - 88%
Same with bilateral synchronies	4	0	9	4 - 44%
Same with delta elsewhere	0	0	9	3 - 33%
Same with other foci	0	0	2	1
No focus	3	0	0	0
Unclassified	0	0	2	0

It is of interest that when the electroencephalogram indicated a localized discharge with secondary conduction of the abnormal waves to the opposite side, the prognosis for a good result with excision was excellent, 88 per cent But it is to be observed that in five such cases the surgeon was unable to decide what area to remove, probably because of the lack of gross abnormality

Electroencephalography in the hands of an experienced interpreter prevents the surgeon from operating upon patients who suffer from idiopathic epilepsy The finding of a three per second dysrhythmia typical of "petit mal epilepsy" is a contraindication to operation More rapid bitemporal dysrhythmia may prove, on analysis, to be due to a unilateral lesion deep in one temporal lobe

Only one patient operated upon had an electroencephalogram which was classified as not of epileptic pattern This patient had choreoathetosis with focal seizures Her electroencephalogram showed an increased amplitude

of beta rhythm over the central area on the right side. Removal of the arm area did not stop her seizures but cured the involuntary movements. Recent electroencephalograms in this case have suggested a deep temporal lobe focus for the seizures.

**11 Postoperative Electroencephalography** Postoperative electroencephalograms were taken in the case of 56 out of the 59 patients after their cortical excisions. This was done in the third or fourth week following operation and after the withdrawal of phenobarbital for 48 hours. Further records were made months or years after operation on some of the patients, but these are too few to be of statistical value and are not included in this report.

The postoperative electroencephalograms taken thus before leaving hospital are tabulated in Table VI. The criteria of improvement, as established by

TABLE VI  
POSTOPERATIVE ELECTROENCEPHALOGRAMS AND PROGNOSIS

Postoperative E E G	Patients	Success Groups 3+4
A Normal	11	9 - 82%
B Much improved	16	16 - 100%
C Slightly improved	9	3 - 33%
D Unimproved	11	2 - 18%
E. Severe delta	9	2 - 22%

Doctor Jasper, were diminution in amount and amplitude of sharp waves, spikes and rhythmic slow waves. A normal record indicates no sharp waves nor spikes. Minimal random slow waves are not considered abnormal in the first few weeks postoperatively.

If the first group—A—and the second group—B—in Table VI are taken together, there are 27 cases in which the postoperative electroencephalogram gave a normal or much improved record, and 25 of these patients had a successful result of operation. On the contrary, little or no immediate improvement in the postoperative electroencephalogram gives small promise of a good result. In retrospect, it seems likely that further excision should have been considered in some of these cases before discharge.

**12 Postoperative Complications** Various postoperative complications to which the neurosurgeon may "fall heir" are summarized in Table VII. Of the patients who had cortical excision, 14, or 25 per cent, had one or more convalescent seizures while in hospital. Of these, five, or 36 per cent, had a Group 3 or 4 result, but only one of them was in Group 4 with complete freedom from attacks. In the control group (not included in Table III) where no excision was made, ten patients, or 71 per cent, had postoperative attacks during convalescence, and none of these had a satisfactory outcome.

Six patients had a second operation for further removal of epileptogenic tissue. One of these had a satisfactory result, and two of them a perfect result.

**13 Medication** Before operation, the best known forms of conservative medication and treatment were given a fair trial. In every case this included

phenobarbital and almost always dilantin. After operation, phenobarbital was given in most cases for a year or more, and if a seizure occurred, it was continued indefinitely. Of the 15 patients who have been completely free of seizures, eight are taking no medication whatsoever, and the remainder take anti-convulsant drugs irregularly as a precaution. Of the 18 who are in Group 3, all but one are taking phenobarbital regularly.

14 *Economic Results* All but one of the 33 patients in the success Groups 3 and 4 are working or studying full time, he has a paralysis of one arm and will be able to work when he learns a trade. Two require supervision because of occasional behavior difficulty. Among those with better results are two physicians, six university students, one school teacher, two stenographers and one professional musician. Even in Group 2 with only a 50 per cent improvement, it is possible for some patients to be economically self-supporting.

TABLE VII  
POSTOPERATIVE COMPLICATIONS AND PROGNOSIS

Complication	Excision Cases	Success Groups 3 + 4
Convalescent seizures	14	5 - 36%
Reoperations further excision	6	3 - 50%
Reoperations for bleeding	3	2 - 66%
Aseptic meningitis	5	4 - 80%

15 *Analysis of Failures* There were 18 patients, or 30.6 per cent, who were not helped appreciably by cortical excision. At operation the removal was considered satisfactory in only three. In the other 15 the lesion was too diffuse for complete removal, or else complete removal would have probably resulted in paralysis or aphasia and thus rendered the patient worse after operation than before.

The 16 patients of the control group, who were operated upon but for whom no cortical excision was deemed advisable, are also to be considered failures. In three, a subtemporal decompression was carried out, in three, lysis of adhesions, in one, removal of a calcified subpial mass, and in one, removal of a calcified subdural hematoma. The diagnoses in this group were hyperostosis frontalis interna, two, craniostenosis, one, arteriovenous aneurysm, one, focal atrophy of brain, three, calcified subpial mass, one, calcified subdural hematoma, one, and no objective lesion, seven.

Postoperative electroencephalograms were taken in 15 of the 16. In none of these was there any appreciable electrographic improvement, and none of these patients could be placed in result Groups 3 or 4, although two felt that they had been helped as much as 50 per cent and were therefore placed in Group 2. Two patients were helped as much as 50 per cent and one slightly improved. Thus, 13 out of 16 were not helped at all. This would seem to indicate that craniotomy which does not include removal of abnormally functioning cortex has no chance of success.

D CASE STUDY

Patients who suffer from epileptic seizures can be studied by means of a simple classification. As information accumulates, it may be necessary to shift the individual from tentative classification under one heading to final classification under another (Table VIII).

1 *Classification*     a **Idiopathic Epilepsy**     In this class the electroencephalogram shows a bilateral disturbance in brain potentials of characteristic form. The seizure begins with loss of consciousness, and when small is of the type recognizable as "absence" or "petit mal." There is often an epileptic tendency in the families of such patients. For idiopathic epilepsy there is no effective surgical therapy.

TABLE VIII

WORKING CLASSIFICATION

- A    Idiopathic epilepsy
- B    Cerebral seizures  
      Cause
- C    Focal cerebral seizures  
      Localization  
      Cause

b **Cerebral Seizures**     When the attacks are not clearly of the above type, the cause should be sought and the pattern of attack studied. If the cause proves to be due to hypoglycemia, to a degenerative condition of the brain, systemic disease, etc., surgical therapy is likewise not indicated, and the diagnosis is expressed, for example, as cerebral seizures, cause—hypoglycemia.

c **Focal Cerebral Seizures**     When the beginning of the seizures is clearly identified and if the cause is obviously not hereditary, metabolic, degenerative or neoplastic, then the diagnosis of focal cerebral seizures may be made. If conservative treatment does not control the attacks, then surgery may be given due consideration. In most cases the patient should be hospitalized for study so that the suitable cases may be selected.

2 *Attack Pattern*     Almost all patients have minor as well as major seizures. The nature of this minor attack or of the earliest beginning of the major seizure gives the observers a clue as to the site of origin. If this is a visual phenomenon, the epileptogenic focus is in the occipital lobe, if it is Jacksonian motor, it is in the precentral gyrus, if sensory, it is postcentral, if hallucinatory, it is temporal, if it begins with unconscious turning, it is one frontal pole, etc. (See Selected Writings of J. Hughlings Jackson, 1931, Penfield and Erickson, 1941.)

3 *Roentgenography*     Asymmetry of the skull or cranial hemiatrophy may be strongly suggestive of birth injury. Cranial defects or depressions and intracranial calcifications may, of course, be highly significant.

4 *Pneumoencephalography*     Ventricular study usually shows some evidence of local cerebral atrophy. That portion of the ventricle must be clearly

visualized which lies under the area of cortex incriminated by the seizure pattern

5 *Electroencephalography* Special methods of electrographic study make it possible to identify the location of epileptogenic discharge in a very high

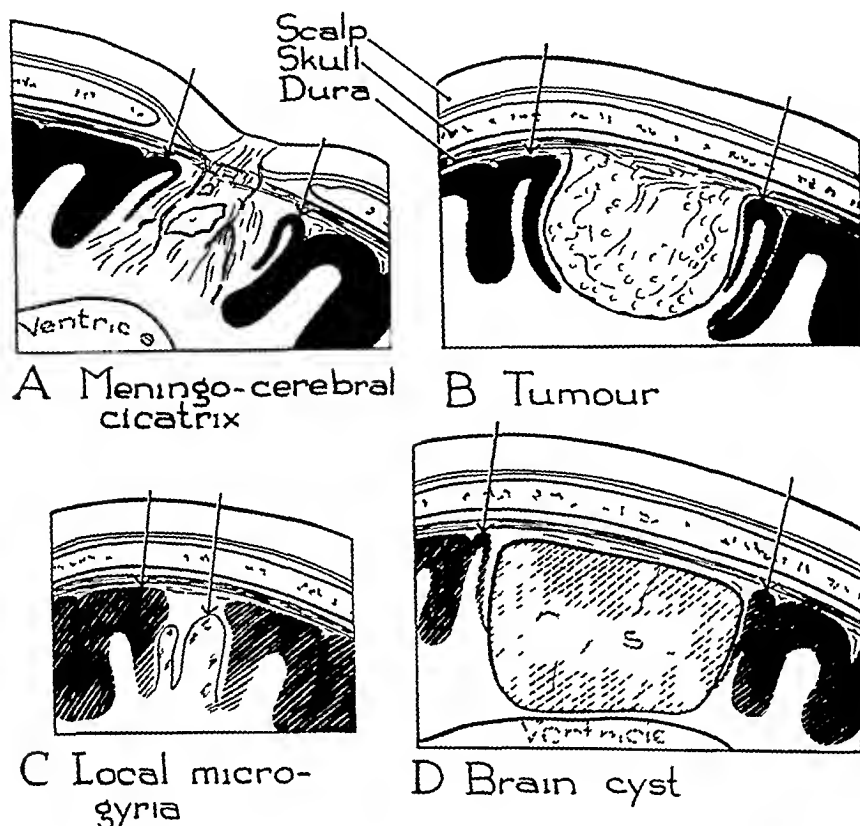


FIG 1—Schematic cross sections of lesions apt to produce foci of epileptogenic discharge in the cerebral cortex. The arrows point to frontier portions of gray matter in A, B and D in which the convolution is partially destroyed. Such gray matter is apt to become the source of seizures, not all around, but only on one side of the lesion. In C, small gyri are shown containing a reduced number of ganglion cells. Such gyri result from local ischemia at birth (from Penfield, W Chapter in *British Surgical Practice*, London, Butterworth, 1947)

proportion of cases of focal epilepsy (Jasper and Penfield, 1943). It is sometimes necessary to make repeated trials and to increase the activity of the focus by artificial means, such as hydration, hyperventilation, metrazol. (See Cure, Rasmussen and Jasper, 1947)

A large area of brain may be abnormal and yet the discharging focus be present in only one small area. The electroencephalogram may thus be the surgeon's best guide. For example, in the case of T K there was a large traumatic lesion of the right frontal lobe. The electrographic record showed the presence of spike discharges, as illustrated in Figure 2, when the electrodes were placed on this portion of the scalp. Three weeks after radical

operative excision, the spike disturbances had disappeared and the record was nearly normal (Fig 3) This patient has had no further seizures after seven years

On the other hand, following brain damage, and also following brain operations, an unfavorable electroencephalogram may continue for years in the

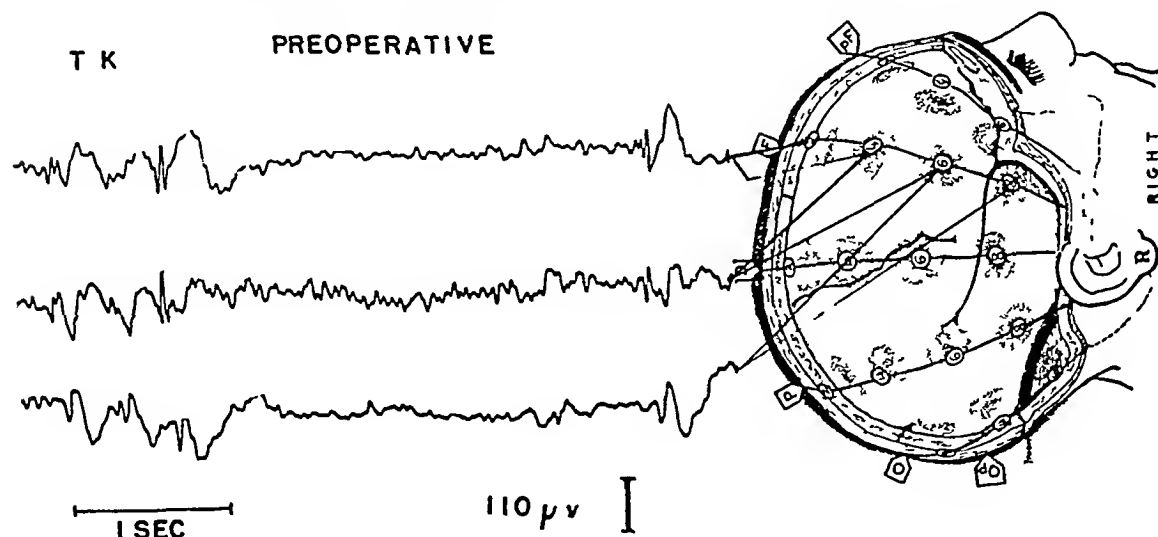


FIG 2—Case T K Electroencephalogram from scalp leads F2, 4, 6 and 8 The “spike” waves indicate a superficial epileptogenic focus

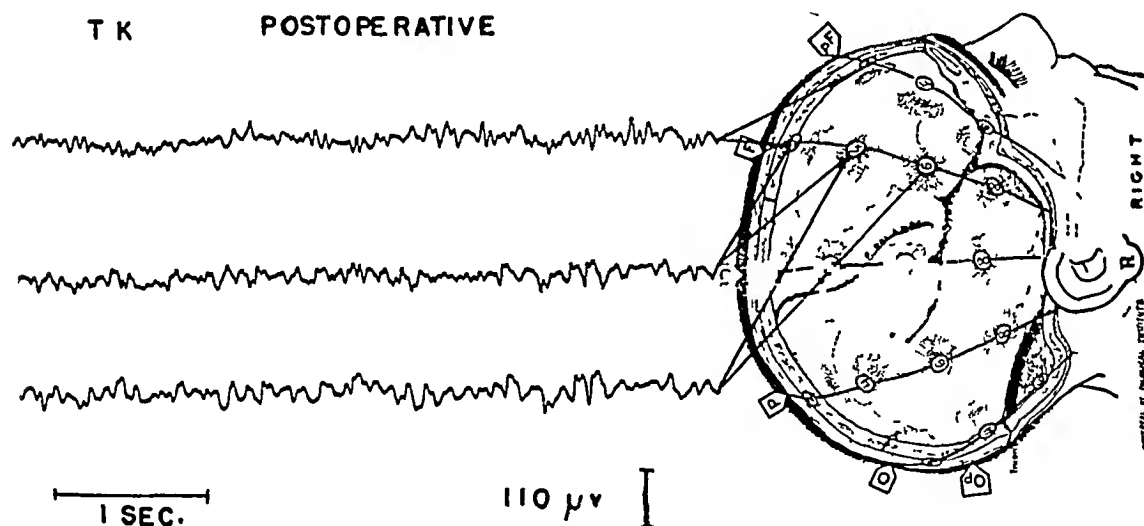


FIG 3—Same case as in Figure 2 Electroencephalogram from scalp leads PF2 and F2, 4 and 6 after removal of cerebral scar The “spike” forms have disappeared

absence of seizures Therefore, the electrographic report alone does not justify surgical interference Furthermore, the electroencephalographer can not predict with certainty whether injured brain will eventually develop into an epileptogenic focus

#### E OPERATION

No preoperative sedative is used and nothing more than codeine during operation An osteoplastic craniotomy of adequate size is made under local



analgesia (Fig 4) The dura is opened with great care so as not to injure the pia mater If very dense adhesions are present, it is well to be sure that only that portion of brain is exposed which is likely to be removed An electrographic study carried out upon the unopened dura is often a help in such a case



FIG 4—Case R E Craniotomy Note line of fracture in the parietal bone, also the defects in the dura corresponding to erosions in the under surface of the bone flap Exposed brain regularly produces such absorption of overlying skull

When the brain is exposed the surgeon faces the problem of what area should be removed He must bear in mind that the actual focus is usually a partly destroyed or atrophied gyrus still capable of function, however abnormal As a preliminary, he should discover where the motor gyrus is by stimulation He may try to induce the patient's aura or minor seizure by stimulation

In the case of R E (Fig 5) the point of maximum injury produced in the

cortex by the depressed bone fragment was obvious. Some study was required to discover how wide the excision could be without producing paralysis and how wide it needed to be in order to ensure relief of seizures.

Electrical stimulation of the cortex was therefore carried out, care being



FIG 5—Case R E. Brain exposed. Numbers on paper tickets mark points from which motor or sensory responses were produced by stimulation. Letters indicate points at which cortical electrographic recording showed "spike" activity. A black thread has been placed on fissure lines up to which excision of convolutions was proposed.

taken to avoid production of a motor (physiologic) seizure. A Rahm stimulator\* is useful for this purpose, frequency 60 per second, beginning with  $\frac{1}{2}$

\* This stimulator was modified by Rahm after the original model described by Rahm and Scarff (1943). The modifications were outlined by Dr. Herbert Jasper and the electrical characteristics are as follows. It is a thyratron circuit providing a saw tooth wave form at frequencies of 1, 3, 8, 15, 30, 60, 90, and 120 pulses per second. The pulse duration is increased with a decrease in frequency of repetition to a maximum duration of 50 milliseconds at the lower frequencies. Stimulus intensities between 0 and 11 volts (peak) are read directly from a meter placed across the stimulating electrodes. A low output impedance permits considerable variation in resistance between the electrodes with minimal changes in stimulating voltage.

volt and increasing to one or two volts. The patient will report sensation from stimulation of the postcentral gyrus or movements may be produced by stimulation of the precentral gyrus. There is no other way of being sure where the central fissure is. In Figure 5 small paper tickets have been placed on points where stimulation produced responses. For example, 1 = movement of left shoulder, 4 = pins and needles sensation in left shoulder, 5 = sensation in left hand, 13 = sensation in left side of tongue, etc. The position of the central fissure was therefore clear.

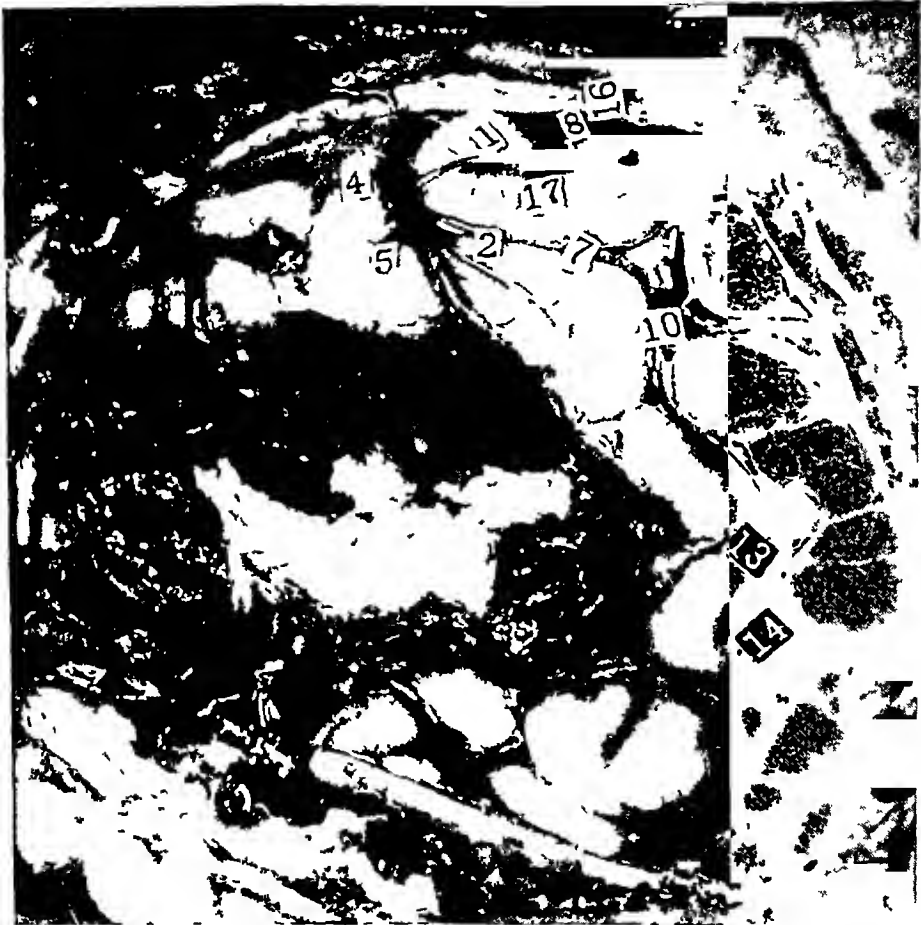


FIG 6—Case R. E. After the excision. Note that the remaining gyri are still covered with pia mater and pial vessels.

An electrocorticogram was carried out, placing electrodes directly on the brain. This showed a good deal of active "spike" discharge about the center of the lesion at B, C, D, F and H. It was decided, therefore, to make a wide excision along fissure lines, and a black thread was placed on the brain as a reminder of the proposed extent of removal. A circular incision was then made inside this line in the convolution between the thread and the central area injury. This incision was made by passing sutures through the pia mater and

then cutting the convolution by tying the suture. The central area was then taken out by undercutting with a dissector. This left behind a half centimeter of convolution about the area of excision. This remaining portion of the convolution was then removed subpially by means of a small sucker in such a way as to leave untouched the pia mater that covered the adjacent gyrus. The result is shown in Figure 6.

During the removal, the patient may be examined to determine whether function has been altered. At the end of the removal he is allowed to go to sleep with the aid of avertin or pentothal\*. The dura is closed, the bone flap replaced and fastened with steel wire. A drain is often placed in the extradural or subdural space and brought out through a small separate incision in the scalp to be removed after 24 hours.

By this technic it is possible to remove all gray matter that has lost its pia in so far as this is possible. It leaves the white matter exposed at the base of the excision. An effort is made not to open the ventricle but to leave ependyma intact. An open ventricle in such cases is apt to produce postoperative fever (aseptic meningitis).

Large excisions may present special difficulties. In the case of D. G., the right occipital lobe was largely destroyed by a subdural hematoma and cerebral compression at birth. When the lobe was exposed at operation (Fig. 7), subdural adhesions were cut and a zone of electroencephalographic "spike" activity was demonstrated, as shown by letters A, B, C, D, and E. The whole lobe was then amputated, leaving a fairly well preserved convolitional frontier. It was not possible to spare the ependyma. Consequently, the ventricle and choroid plexus are seen to be exposed.

The postoperative course was stormy. The wound was reopened to evacuate an extradural hematoma. This was followed in turn by a scalp infection which was treated and then closed secondarily. A prolonged period of aseptic meningitis followed. Nevertheless, healing was eventually satisfactory and the boy has been free of seizures during the two and one-half years since operation, and certain behavior difficulties have disappeared along with the seizures, an added benefit which is not uncommon.

#### F. EXCISION TECHNIC

Horsley (1909) first described the subpial method of convolitional removal, and Sachs (1935) and Furlow (1938) endorsed it. Foerster (Foerster and Penfield, 1930) used the method of cutting with a thread, the line of excision being made down the middle of each convolution as far as possible, thus leaving half of the convolution. Penfield used the same method for the 115 patients operated upon in the 1929 to 1939 period (Penfield and Erickson, 1941).

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\* Dr. Ronald Stephen (our associate in charge of anesthesia) finds that avertin tends to drop the pressure too much at the close of operation. He prefers sodium pentothal intravenously, combined with a 50-50 mixture of nitrous oxide and oxygen administered through a nasopharyngeal tube, using a non-rebreathing valve. Most patients required an intravenous saline infusion, some a transfusion.

In the present report the removal method is a modification of the two, the central area being excised by the thread method and the peripheral zone being cleaned out subpially by suction. The results in this series are 12 per cent better than in the earlier series, but that does not necessarily demonstrate that the improvement is due to the altered technic of removal.

More accurate indication of the success of excision technic may be found in the postoperative electrogram. In 19 of the excision cases (17 per cent), the electrogram gave evidence that remaining gray matter had been damaged at

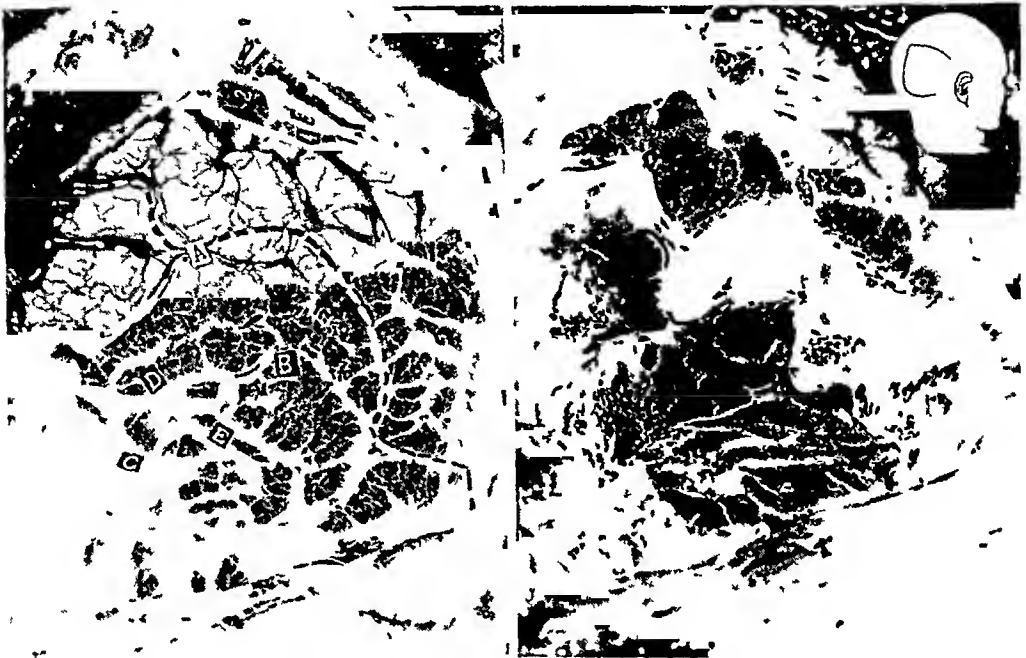


FIG 7—Case D G. On the left is shown the occipital lobe injured at birth. A, B, C, D, and E indicate electrographic evidence of epileptogenic activity. Numbers 2, 3, and 4 lie on the postcentral gyrus, as proved by stimulation. The broken line indicates the limit of proposed removal. On the right the removal has been carried out, consisting in an occipital lobectomy. The ventricle, unfortunately, had to be opened.

operation or that it had had its circulation interfered with. This was indicated by the presence of large slow waves (delta waves). Only two of these patients, or 22 per cent, had a satisfactory result. The conclusion seems to be that for these 19 patients there was either some imperfection in the execution of the technic or that a better technic should be devised so that no delta waves appear after operation. When a surgeon is able to pass the test of the postoperative electrogram, he may claim that his technic of excision is satisfactory.

#### G SUMMARY AND CONCLUSION

There is a large group of patients ordinarily treated on a symptomatic basis as essential epileptics. Some simple working classification, such as that in Table VIII, should be used to distinguish these sufferers from those that are

subject to cerebral seizures due to systemic abnormality or to idiopathic epilepsy. In the differential diagnosis of such patients the terms "grand mal" and "psychomotor epilepsy" are confusing unless it is recognized that they refer to electroencephalographic patterns with no particular clinical significance.

In this present series of 76 patients, there was one death (1.2 per cent operative mortality). Of the 59 patients who had excision, 15 had no further attacks during a one to seven year postoperative period (Group 4), and 18 had one or two seizures but considered themselves cured or practically so (Group 3). Adding the two groups together, 56 per cent of the patients had a successful operation. Sixteen similar craniotomies were carried out without excision and none of these was successful (Table I). It therefore seems fair to conclude that epileptic seizures, due to cerebral abnormality, are not helped by craniotomy unless radical excision is carried out. Removal of adhesions, decompression, or closure of cranial defects have no effect upon the attacks unless the proper excision is carried out.\*

The elements of success or failure in the excision series are to be sought in an analysis of the nature of the lesion, the methods of study, and the technique of removal.

The cause of the original lesion in this series was most often head injury, secondly, birth injury, and, thirdly, local infection. The cause was unknown in 12 per cent of the excisions and in 62 per cent of the negative explorations (Table II). The duration of attacks before operation had little or no influence on the outcome (Table IV).

It is interesting that when the cause was head injury or infection, the onset of seizures was early. The beginning of attacks in these cases came within five years in four out of five cases. On the other hand, when the cause was birth injury, the onset of seizures was longer delayed. The beginning of attacks came after the age of five in four out of five cases. It would seem, therefore, that during infancy and early childhood damaged brain is usually slower to develop the epileptogenic mechanism than later in life.

The best results from excision were obtained in the birth injury group (76 per cent). Infectious processes came next with 56 per cent success, and head injury third with 51 per cent (Table III). Excision is equally effective when applied to meningocerebral scars or to simple cerebral foci. Removals in the frontal pole were most successful (73 per cent), and the central (or sensorimotor) cortex came next (67 per cent).

When attacks recur after operation and after the patient leaves hospital, the earlier they appear the more gloomy is the prognosis of eventual recovery. When attacks occur in the convalescent period while the patient is still in hospital, the prognosis of a good result is extremely poor if the pattern of onset is the same as before operation. Attacks that indicate a neighboring gyrus is subject to edema or anoxemia will have a different pattern and may produce less

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\* When craniotomy without excision results in cessation of attacks, it is likely that the patient should have been classified in the idiopathic group. Such patients occasionally have spontaneous cessation of seizures.

pessimism If the pattern is the same as preoperatively, an immediate second operation should be considered Six patients were thus subjected to a second excision, and three of them were thus placed in success groups (Table VII)

As the result of this present analysis we would conclude that the persistence of a "spike" electrographic focus after operation or the appearance of marked "delta" electrographic activity near the site of removal should cause the surgeon to consider reoperation (Table VI)

In preoperative studies, the simpler the electrographic record is and the better it is localized, the better the prognosis of a successful excision The more diffuse the electrographic abnormality, the less hopeful is the prognosis (Table V) It must be added, however, that a well localized, simple electroencephalogram, not supported by pneumographic or other evidence of a lesion, has sometimes led us to a useless exploration, i e., a craniotomy without excision Excision guided solely by electrographic abnormality seems to be a procedure of doubtful value The uses of electroencephalography during operation (electrocorticography) are still being studied and will be reported upon at a later time

In conclusion, the surest guide to localization of an epileptogenic zone is the seizure pattern The greatest supplementary help a surgeon can receive is electrographic study by an expert,\* and it is fair to say that this special method of study has opened a new chapter in the treatment of focal epilepsy However, the electrogram without objective change in the cortex and without the other means of study is not yet to be trusted as the final guide to excision

Radical excision seems to offer a reasonable possibility of cure (56 per cent) to those who have cortical foci of discharge and whose attacks are not controlled by medication All patients operated upon within a given period have been included in this report, so that the elements of success and failure may become apparent and in the hope that this may prepare the way for future advance

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\* We must express our gratitude to Dr Herbert Jasper, and to his pupil in electroencephalography, Dr John Kershman, for guidance and stimulation in the study of this series

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DISCUSSION—DR GILBERT HORRAX, Boston I think we all owe a great debt of gratitude to Dr Penfield for the work he has done for a long time on the surgical treatment of epilepsy This is such a widespread disorder that any type of treatment that offers relief is most important I think the things for neurosurgeons to remember are these First, careful neurologic study preoperatively so far as history and type of seizure are concerned, second, we ought to have the help of men like Dr Jasper for electroencephalographic interpretation and, third, that the epileptic focus does not confine itself to the area seen at operation but may extend beyond the area, and this should be studied for response to electric stimuli

DR. W J MIXTER, Boston This is a very important contribution Dr Penfield's work we all know, he having had more experience than any of the rest of us in this type of work, and his results are probably better than most of us can have This comes with particular importance at this time, because we have a large number of post-war epileptics in the world today, many of whom are open to treatment along these lines When we consider the number in this country and multiply that by the number there must be in backward countries where there are no means of handling these cases, we can see the load the world must carry in caring for these cases

One thing seems to me of great importance That is the study of encephalography on the open brain which Dr Penfield alluded to I believe this is a very important part of the operation, and I want to stress that fact, because there have been too many of these scars excised without testing the cortex As Dr Horrax said, many of these show extension of the epileptic focus to the side away from the scar, and in such cases simple removal of the scar itself will not cure the patient I would like to hear what is being done in the Veterans Administration concerning this group of cases

DR. W MCK. CRAIG, Rochester, Minn Dr Mixter has referred to the Veterans Bureau and epilepsy Realizing that subsequent to all the head injuries sustained in the last war there would be a large number of post-traumatic epilepsy cases, the National Research Council has endeavored to set up committees and subcommittees to supervise projects in the Veterans Hospitals Follow-up studies are to be carried out and when epilepsy occurs these cases are to be dealt with in a manner similar to that described by Dr Penfield

By his work Dr Penfield will prove a great benefactor to the veterans program and merits our gratitude for his efforts

DR. WILDER PENFIELD, Montreal (closing) I am very glad that Dr Horrax emphasized the importance of electroencephalography It is the greatest aid, although the study of the simple epileptic patterns still remains the most important method of localizing attacks So far as electroencephalographic records from the exposed brain are concerned, we have been doing this for six or seven years but are not ready to make final judgment as to its value. It does help, but it is possible, also, that it may misdirect the surgeon because of the altered condition of the cortex after exposure

Dr Mixter called attention to the great body of post-traumatic cases from the war, the world around During the next five or ten years there will be an enormous number of veterans complaining of post-traumatic epilepsy The attacks are apt to begin any time in the ten years following injury I feel that in Russia the incidence may be higher than here because of their different technic in handling brain wounds They left the brain wound open for a longer period than was the habit here That remains to be seen

Dr Craig mentioned the work with veterans Our feeling in general is that the veteran who has seizures should be treated for at least a year by all possible conservative measures before operation is considered The duration of seizures has no influence upon the eventual result of operation There may be an epileptic habit, but if the focus is properly removed the nerve pattern of habit goes with it

## URGENT SURGERY IN THE AGED\*

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LITTLE AS THE SURGEON may relish major operative procedures on patients in the seventh decade or beyond, there occur occasions when he is forced to intervene to preserve life. With the consistent aging of the population, such occasions may be expected to occur with ever greater frequency.

The Goldwater Memorial Hospital of New York, serving the chronic patients drawn from all the City's hospitals and from the City Home for aged and indigent persons, has furnished opportunity for the observation of surgical emergencies in old people. This review is based on the experiences of the Second Surgical Division over a period of seven years.

The 204 patients who were the basis of these observations ranged in age from 60 to 102. The average age of the group was 74. These patients presented not only the "normal" deteriorations of age, but also many of the diseases of senility in chronic and advanced form.

These factors of deterioration and of disease give the problem of urgent surgery in the older age group its special character. When an emergency arises, there is little opportunity to improve the patient's physical status and none to rectify fundamental organic defects. Frequently encountered in our patients were myocardial degeneration, valvular heart disease, overweight, malnutrition, the results of previous coronary infarction or cerebral vascular accident, tuberculosis, lues, diabetes, anemia, vitamin deficiency states, hypoproteinemia, arterial sclerosis, varieties of renal or hepatic dysfunction, or combinations of these defects.

These conditions often entailed difficulties of early and accurate diagnosis, since the defects might mask or mimic conditions requiring quick surgical intervention. There were also serious postoperative complications. These old patients are peculiarly susceptible to pneumonia, wound disruptions and sepsis. Many of them succumb, even weeks after operation, to cerebral-vascular accidents, to coronary occlusions, uremia, anuria, and cardio-vascular-renal collapse. While the mortality rate attending urgent surgery in this group was high (84 deaths following 188 operations, or 44 per cent), the survivals represent surgical salvage of individuals who, unaided, would almost surely have succumbed. Our attitude was well expressed by Rowntree<sup>1</sup>: "All would agree that every effort should be made to save life in acute emergencies, unless the patient is already in extremis." Of our 204 patients presenting surgical emergencies, 15 were either in extremis or refused surgery, and all 15 succumbed.

Certain general principles of therapy were adopted to meet the requirements of this class of case. (1) Utilize every quickly available measure for support

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\* Read before the American Surgical Association, March 26, 1947, Hot Springs, Va.

and protection (2) Undertake the remedial operation with the least possible delay (3) With a minimum of trauma and in the shortest feasible time, perform the simplest procedure that will relieve the emergency (4) Employ every means to safeguard the patient against postoperative complications and watch diligently for signs of their development

In carrying out the principle of support and protection in the preoperative period, we have tried to take advantage, as they became available, of all valuable measures replacement of depleted fluids and electrolytes, correcting impending acidosis with glucose and insulin, furnishing new blood or plasma, using the hydrolysates to raise the lowered blood protein level, employing concentrated vitamin solutions to promote tissue repair or to minimize hemorrhage, or the anticoagulants in thrombotic or embolic states The antibiotics have proved a powerful ally, and the patient about to be submitted to operation, whether septic or not, should not be deprived of their protective and prophylactic effects Penicillin has become our stand-by (although more than half of our patients were seen before it became available), and it has been our custom to begin its employment preoperatively in doses up to 100,000 units at three hour intervals We have found it important in these elderly patients to recognize the inability of the failing heart and kidneys to deal with large quantities of fluids if given rapidly by vein

While the value of the principles enunciated by Ravdin<sup>2</sup> and by Whipple<sup>3</sup> concerning replacement of weight loss, high caloric diet and the increased administration of food proteins as preoperative safeguards was recognized, time was lacking in these urgent cases to carry them out In our own experience, as in Bailey's,<sup>4</sup> all too often serious ailments were permitted to develop well beyond the margin of safety before surgical opinion was consulted

Supportive measures should not delay unduly the performance of urgent surgery where early intervention is required These old people deteriorate rapidly under sepsis, death of tissue, or obstruction of the intestinal tract Delays in laboratory or X-ray investigations, in ineffective efforts at intestinal intubation or in trying to reach an unattainable optimum in the patient's condition may lead to failure

The choice of appropriate anesthetic is important Depressant or toxic anesthetics are unusually hazardous in the aged We have veered away from spinal anesthesia, apprehending the circulatory depression that frequently attends its use The fear of respiratory depression has deterred us from the barbiturates Chloroform and vinethene have too marked toxic properties, while nitrous oxide anesthesia involves anoxia Cyclopropane proved an almost ideal anesthetic, combining low toxicity, rapid induction and recovery and good relaxation, and permitting high oxygenation Ether we found reliable, reasonably safe, and effective Latterly, intocostin has served to increase relaxation, permitting the use of smaller quantities of cyclopropane or ether We have seen no ill effects from its use

Local anesthesia was useful in many cases, but if it produced toxic effects, prolonged the operative procedure or failed to allay shock-producing pain, it

was inappropriate. Since large doses of morphine as a basic sedative are not well tolerated, we have supplemented smaller doses (gr 1/8) with small amounts of scopolamine (gr 1/150) with satisfactory results. In some cases we have combined scopolamine with demerol (50 mg) with equally good effect. Refrigeration anesthesia for amputations, as proposed by Crossman<sup>5</sup> and Allen,<sup>6</sup> became almost routine after the middle of 1941.

With skilful use of the anesthetics now available, the anesthesia has not constituted a grave risk. In the 188 operations recorded, there was only one fatality in which the anesthesia was involved. Pneumonia, following operation, occurred in about the same relative frequency with each of the types of anesthesia employed, and in roughly half of the cases, appeared ten days or more after the anesthetic.

Our experience parallels that of other observers. Bancroft<sup>7</sup> prefers local or cyclopropane anesthesia. Knight and Baird<sup>8</sup> like local or block anesthesia, but have not been satisfied with them in abdominal operations. Forestiere,<sup>9</sup> anesthetist at the Goldwater Memorial Hospital, states "Results with inhalation anesthesia are not surpassed by those with local, regional or other anesthetic procedures." Rowntree<sup>1</sup> observes that old people take anesthetics well. Quigley<sup>10</sup> found that the type of anesthesia had little or no effect on mortality. Rankin<sup>11</sup> sums up the matter "A good anesthetist, a short operative time and careful postoperative care will render the use of general anesthesia in old people as safe as any other anesthetic available."

Minimum trauma at the operation is nowhere so important as in the poor-risk elderly patient where shock must be avoided. The surgeon learns that he must be both accurate and fast, although as Rowntree<sup>1</sup> puts it, "Better an hour or more of gentle manipulation than five minutes of clumsy bungling."

The emergency operation on the old patient should be the least and simplest procedure that will meet the issue. Once the emergency is passed, the patient may be prepared under far more favorable circumstances to undergo any additional operation required. Elective resections and anastomoses, meticulous repair of hernias, prolonged exploration of the common bile duct and plastic amputations have no proper place in emergency surgery on old people. As Rankin says,<sup>11</sup> "The nicety of surgical judgment as to when, what and how much to do is the keynote to success in these patients." During the course of the emergency operation, continuing support and protection of the patient are important. Most valuable, as Wangenstein<sup>12</sup> suggests, is the replacement of all blood lost by administration of blood, or at least by plasma.

During the early postoperative hours, shock has been our first concern. Our chief reliance in combatting it has been in the use of blood and oxygen. It has been our practice to continue oxygen for at least six hours after operation, and for several days in some instances. Stimulant drugs have been, in the main, disappointing. Postoperative sedation must be cautiously managed.

To prevent atelectasis, thorough aeration of the patient has been regularly performed at the close of the operation and during the succeeding 24 hours, rebreathing procedures carried out. Nurses were instructed to move and turn

the patients frequently, to assure that a free air-way was maintained and that no aspiration of vomitus occurred. These measures, plus the continuance of penicillin, are the best insurance also against pneumonia. The termination of bed rest at the earliest possible moment has been our policy since the start of our service. This practice no doubt has had value in preventing phlebo-thrombosis and decubitus. In our patients who were out of bed early we encountered no instance of wound dehiscence. This accident occurred more frequently in patients who of necessity remained bedridden and was the product of distention, sepsis, wound infection, vitamin deficiency, lowered blood protein or the presence of carcinoma, rather than of the muscular action produced by early rising.

Closely spaced through-and-through retention sutures in abdominal closure seemed to provide the best safeguard against disruption, supplementing careful repair by layers, special attention being given to accurate closure of the peritoneum. Special effort was made to provide optimum nutriment and to correct anemia, metabolic disturbances and deficiency states.

Fortunately phlebo-thrombosis has been rare. Our present policy is to ligate and divide the superficial femoral vein of the leg showing involvement. If cryptogenic embolization occurs, we rely on heparin plus dicumarol.

Attention to moving, keeping the patient dry (for many of them were incontinent), early ambulation, avoidance of pressure and maintenance of nutrition sometimes failed to prevent decubitus. When ulcers occurred, we were unable to reproduce in these old patients the brilliant results of plastic closure or grafting that we saw in the young victims of decubitus during the war.

A factor in the recovery of the old person who has undergone urgent surgery is the will to live. Rankin<sup>11</sup> emphasizes the bad effects of "regimentation and the domination of a relentless and impersonal routine." Lacking encouragement or an alert and sympathetic interest in their complaints, having no incentive and no outlook to a less miserable future, sick old people are prone to lapse into a state of unresponsive indifference and lethargy from which a terminal pneumonia usually provides the ultimate release.

The general principles above outlined may be illustrated by citing the more common surgical emergencies we encountered.

#### AMPUTATIONS

The emergency most frequently met was gangrene of the lower extremity, associated with arterio-sclerotic occlusion, with or without diabetes. Usually there was premonitory complaint of pain in the extremity and evidence of diminished arterial circulation. The onset of the complete occlusion was heralded by increased severity of the pain, cyanotic pallor of the affected part, and coldness. We encountered no case of embolic occlusion in which it was feasible to attempt embolectomy.

The obvious death of one toe or more, or a part of the foot or leg, did not constitute an emergency. Conservative treatment awaiting demarcation was then in order. If spreading infection in the extremity became apparent with

elevation of temperature, rapid pulse and an ascending flush or lymphangitis, amputation became urgent. Local incision or amputation anywhere within the zone of active cellulitis served only to make a bad matter worse. A lower-third or mid-thigh amputation was the proper treatment, and the sooner employed the better.

Penicillin was administered in large doses, blood for transfusion procured, and the infected extremity segregated by tourniquet and local refrigeration begun. Crossman's<sup>5</sup> technic proved most effective and we rarely found it necessary to employ any other anesthesia. Following the application of tourniquet and ice, the patient's condition generally improved. This procedure put a stop to the spread of sepsis at once and gave three hours or more of refrigeration to devote to preparatory, corrective and supportive treatment. As a means of anesthesia the method in our hands was not superior to other anesthetics in the matter of operative risk or postoperative complications.

In septic cases, flap-forming procedures resulted often in septic and necrotic stumps and were abandoned in favor of the circular type of amputation. Loose closure of such stumps has been, until recently, our method, but a high incidence (60 per cent) of the breaking down of these wounds dictated the adoption of the completely open treatment with the application of skin traction, as advocated by Kirk for war injuries. With this method we have seen less suppuration and spreading infection in the stump. Applied with a plaster cuff and outrigger, such traction does not require bed confinement. One reason for the ineffectiveness of flaps and sutures has been demonstrated repeatedly at the operating table where, even at a generously high level, the main artery has been found completely obliterated by sclerosis and organized clot and the compensatory circulation so meager as to produce very little bleeding.

In patients suffering from diabetic gangrene there may, or may not, have been premonitory evidence of progressive peripheral circulatory failure. Invasive infection, with following cellulitis and gangrene gained access through an abrasion or dermatophytosis of the foot, from a closely cut corn or around an old horny toenail. Bringing the blood sugar under control in some instances served to localize the infection. Surgical treatment then was conservative. Where the infection was advancing, amputation was called for.

There were 73 cases of gangrene of the extremities. The average of these patients was 72 years. All showed evidence of arterial sclerosis, while 62 had clinical manifestations of arterio-sclerotic heart disease. Twenty-nine, or more than a third of them, had diabetes. Fulminating sepsis was present in 45. Fifteen were nephritic, 12 had had cerebral accidents and 17 suffered from coronary disease. Five had had previous leg amputations for gangrene. Among the other complications, which in most cases were multiple, were fractured femurs, leg ulcers, decubitis, active tuberculosis, anemia, prostatism, gastric ulcer, syphilis, rheumatic heart disease, bacterial endocarditis, pericarditis, cirrhosis, pneumonia and empyema, while one patient was recovering from an operation for acute intestinal obstruction.

Eight of the 73 either refused operation or were inoperable All of these succumbed

Incision and drainage of suppurating areas about the foot or the amputation of gangrenous toes was followed in 20 cases of the 65 by obligatory thigh amputation within a few days We gained a distinct impression that it was often a precipitating factor

Of the 65 operations performed, 59 were mid-thigh amputations, four were of the Carden type One of these required subsequent mid-thigh amputation for sepsis Two amputations were below the knee One of these developed gas gangrene demanding a mid-thigh amputation four days later Fifty-six operations were of the circular type, while three were done with flaps Forty-six had light suturing of muscle and skin over the bone end and 30 of these stumps suppurated, two with gas infection The skin alone was loosely sutured in 16 cases and broke down in six Thus 60 per cent of the sutured stumps broke down, leading to the present tentative practice of leaving open stumps with skin traction in septic cases This may prove to be too conservative, but thus far we have been pleased with their healing by granulation

Other postoperative complications were Pneumonia, 22, sepsis, 6, shock, 3

For anesthesia, cyclopropane was used in 20 cases, spinal in ten Most of these were given prior to 1941, as was one nitrous-oxide-oxygen anesthesia Since the introduction of refrigeration anesthesia, most of the amputations

TABLE I  
GANGRENE OF EXTREMITY  
Number 73 Average Age 72

Preoperative Condition	Amputations 65	Postoperative Complications
Arteriosclerosis 73	Thigh 59	Pneumonia 22
A S H D 62	Carden s (knee) 4	Sepsis 6
Diabetes 29	(1 reamp for sepsis)	Shock 3
Sepsis 45	Below knee 2	
Nephritis 15	(1 reamp p 4 d —gas)	Recovered 40
Cerebral accident 12	Circular (guillotine) 56	Died 25
Coronary disease 17	With flaps 3	Mortality 38%
Decubitus 12	Suture of muscle and skin 46	Day of death (av) 11
Pneumonia 4	Broke down 30	Cause of death
Tbc 2	(2 gas infections)	Pneumonia 11
Lues 2	Suture of skin only 16	Sepsis 1
Fractured femur 4	Broke down 6	Shock 3
Leg ulcers 5		Decompensation or coronary 6
Previous major amputation 5	60% of sutured wounds opened	Cerebral accident 2
Septic endocarditis 1		Bleeding gastric ulcer 1
Pericarditis 1	Anesthesia	Gangrene other leg 1
Empyema 1	Cyclo (Pn 8—40%) 21	
Acute intestinal obstruction 1	Spinal (Pn 3—30%) 11	
Cirrhosis 1	Crymal* (Pn 9—30%) 31	
Gastric ulcer 1	N <sub>2</sub> O (Pn 1 ) 1	
Prostatism 7	* Supplemented with	
Severe anemia 8	Vinethene (1)	
	Cyclo (1)	
	Pentothal (1)	

8 unoperated—all died

No anesthetic accident

(31) have been done with it. There have been no anesthetic accidents. Pneumonitis occurred in 40 per cent of the cyclopropane cases, in 30 per cent of the crymal anesthetics, and in 30 per cent following spinal. Six of eleven fatal cases of pneumonia occurred ten days or more after the operation.

Of the 65 patients operated upon, 40 recovered and 25 died—a mortality rate of 38 per cent. The average day of death was the 11th. Three cases of shock died within 48 hours, the other victims at intervals up to one month. Pneumonia took the highest toll of 11 lives. Sepsis claimed one, cardiac decompensation and coronary accidents killed six, cerebral hemorrhage two, and bleeding gastric ulcer and gangrene of the other leg one each. The operated diabetic patients showed as good a recovery rate as did the non-diabetics.

#### INTESTINAL OBSTRUCTION

Among the causes were incarcerated and strangulated hernia, carcinoma of the large bowel, adhesions causing kinks or volvulus, foreign bodies, mesenteric thrombosis, and fecal impaction.

The diagnosis of intestinal obstruction in old people and the determination of its cause and location presented difficulties. Since many of them were chronically constipated, the absence of bowel movements for a day or two was likely to pass unnoticed. The complaint of some abdominal discomfort might easily escape attention, or the combination of the two situations might elicit an enema or a cathartic. These people not infrequently developed atonic colons loaded with fecal matter, often associated with massive rectal impaction, which produced a degree of intestinal obstruction. In such instances the enemas and cathartics usually relieved the situation.

Two or three days might pass after the onset of a true obstruction, particularly if it were in the large bowel, before the development of distention and vomiting led to the calling in of the surgeons. Our cases of obstruction were often well advanced by the time surgery could be employed. Faced then with an emergency, little time was permitted for investigation. We adopted the policy of instituting early surgical treatment for such patients as rapidly as the necessary replacement and supportive therapy could bring them to a state of operability. Dehydration and electrolyte deprivation were corrected, plasma given and blood administered or procured. A digital rectal examination was done, and three-position X-ray films of the abdomen were made to detect fluid levels and identify the distended loops of gut. This was sometimes supplemented by a barium enema picture. Such studies often proved helpful in determining the most direct approach and the shortest procedure, obviating an extensive exploration. With the insertion of a tube into the stomach and suction decompression established, the patient was ready for operation.

(1) *Large intestine tumors*. In obstructive lesions of the large bowel, only cecostomy or colostomy was usually required. This might be done under local anesthesia. In performing a cecostomy through a right lower quadrant muscle-splitting incision, the withdrawal of a good segment of cecum through the skin was preferred. No opening was made in the gut until the wound had been



closed and protected. Then a tube of good size or Pessier catheter was inserted well into the intra-abdominal portion of the gut within a purse-string suture.

When a large bowel tumor was demonstrated at exploration through a rectus incision, this incision was closed and cecostomy performed. We learned the unwisdom of attempting to deal with the new growth itself, even by exteriorization, in the presence of acute obstruction.

(2) *Ileus of small intestine* In obstructions of the small intestine, the symptoms were usually more lively in onset, leading to earlier recognition. Preoperative speculation proved fruitless in estimating the nature of the lesion. One might find a constricting band, kinks, volvuli, or internal hernia, with or without gangrene of the intestine, or even an obstructing foreign body. We were unable to differentiate before operation the cases of mesenteric thrombosis from those of mechanical ileus.

We found a generous incision to be a sound investment. Once found, the obstruction was relieved as rapidly and with as little handling as possible. When the gut was found to be definitely gangrenous, exteriorization of the affected loop gave the best chance of immediate survival, but involved the dangers resulting from intestinal fistula. When the lesion was in the jejunum or upper ileum, an anastomosis seemed obligatory. In the low ileum, exteriorization might be done with spur formation and later effort at restoration of continuity.

(3) *Hernia* Incarceration or strangulation of intestine brought the occasional hernia into the field of urgent surgery. In cases of suspected obstruction, a small hernial sac might easily be overlooked. In the operation we preferred an abdominal approach if there was likelihood of gangrenous gut in a sac. Relief of the obstruction and adequate management of the gut was the primary purpose in such operation, and repair of the hernia, other than closure of the internal orifice, was not important. Release of the gut and protection of the peritoneum from spilling of intestinal contents was more surely to be accomplished by the abdominal route.

The postoperative care of patients recovering from intestinal obstruction consisted of suction through the stomach tube while distention or vomiting persisted, plus supportive and nutritive treatment. The patients were taken out of bed within the first 24 hours, or as soon thereafter as possible.

Of our 56 cases of intestinal obstruction, 52 were operated upon, while four were received in such condition that operation could not be undertaken. Twenty-four patients were operated upon within 24 hours of the onset of the symptoms, while others were not seen until two, three, four or five days after the beginning of obstruction. The average duration of symptoms was two days. These patients averaged 81 years of age. The oldest, who made a complete recovery, was 102. Forty-seven were markedly arterio-sclerotic and 37 showed gross clinical evidence of arterio-sclerotic heart disease. Seven had had cerebral accidents (one had suffered two), and five had previous coronary thrombosis. Nephritis, cirrhosis, pulmonary tuberculosis, paralysis agitans, central nervous system lues, crippling arthritis, prostatism, pyelo-nephritis, carcinoma

of the bladder, spinal cord tumor and recent amputation for arterio-sclerotic gangrene were some of the preoperative complications

Twenty-three of the obstructions were due to strangulated hernias, 11 to cancer of the large bowel, nine to adhesions, five to volvulus, three to foreign bodies (one gall stone, one peach stone, one meat bone—perforated), one to lymphopathia venereum, while the causes of two were never determined

Operation in 29 instances consisted in reduction of hernia, volvulus, or freeing of constricting bands Four small intestine resections were done There were 11 cecostomies, two colostomies and one ileostomy with exteriorization of loop Cyclopropane was the anesthetic used in 22, local in 20, pentothal in two, ether in three, and spinal in five There was but one anesthetic death, which occurred from aspiration of vomitus in one of the spinal cases Spinal anesthesia was administered in some of our earlier cases but we are now opposed to its use in patients of this type

The mortality was high Twenty-three survived, while 29 died, giving a rate of 55 per cent Pneumonitis was responsible for 13 deaths Six succumbed to shock, six to cardiac failure, two to peritonitis The patients dying of shock or cardiac decompensation succumbed usually within three days Pneumonia killed as late as the 54th postoperative day Other late deaths occurred from ruptured esophageal varices, cerebral accident and uremia

TABLE II  
INTESTINAL OBSTRUCTION  
Number 52      Average Age 81

Preoperative Condition		Cause		Anesthesia	
Arterio-sclerosis	47	Hernia	23	Local	20
Arterio-sclerotic		Inguinal	11	Cyclopropane	22
Heart disease	37	Femoral	5	Pentothal	2
Cerebral accident	7	Incisional	2	Ether	3
(One had 2)		Umbilical	5	Spinal	5
Coronary thrombosis	5	Adhesions	9		
Nephritis	12	Volvulus	5	Postoperative Complications	
Cirrhosis	1	Neoplasm of colon	11	Pneumonia	17
Urological		Foreign body	3	Peritonitis	2
Prostatism	4	(Gall stone 1)		Shock	7
Pyelo-nephritis	2	(Peach stone 1)			
Carcinoma of bladder	1	(Meat bone 1)			
Lues	2	Lymphopathia	1	Cause of Death	
Decubitus	3	Undetermined	2	Pneumonia	13
Arthritis (disabling)	4			Shock	6
Tuberculosis	2			Peritonitis	2
Central Nervous System		Duration		Uremia	1
Disorders		Average	2 days	Cardiac failure	6
Paralysis agitans	4	Less than 24 hours	24	Cerebral accident	1
Cord tumor	1			Aspirated vomitus (anesthetic	
Lues (C N S)	1	Operation		accident—spinal)	1
		Reduction	29	Ruptured esophageal varix	1
		Resection	4		
		Cecostomy	11	Result	
		Colostomy	2	Recovered	23
		Ileostomy	1	Died	30
		Exploration	2	Rate	55%
		Enterotomy	3		
		(Removal of foreign bodies)		Day of death (average)	4

The one best guide to prognosis was found to be the physical status of the patient at the time of his obstructive accident and the nature and degree of his pre-existing ailments. This observation corresponds with the conclusion of Brooks,<sup>13</sup> who noted that a high percentage of deaths in old people after operation occurred late and were due to pre-existing degenerative diseases.

#### APPENDICITIS

Acute appendicitis occurred only five times in 204 cases. (According to van Friedendeldt<sup>15</sup> only 7.2 per cent of all appendicitis occurs in patients over 50.) Its behaviour was likely to be atypical, leading to difficulty in diagnosis. After a few hours of vague abdominal discomfort, without localizing signs, there might appear evidence of peritonitis and at operation a ruptured appendix be found. Or where a palpable right lower quadrant abscess was found, one might elicit the story of an episode of "indigestion" or "stomach ache" a number of days previously. In consequence, the diagnosis was often delayed. We noted, as did de Tarnowsky,<sup>14</sup> the vague nature of the onset and development of appendicitis in old patients, and the frequent and early occurrence of gangrene. We have felt it important to pay strict attention to the older patients' complaint of abdominal pain and to watch with care the blood count, the temperature, and particularly the pulse rate. The abdominal physical signs we have frequently found to be undependable or misleading.

For appendectomy we preferred the intermuscular right lower quadrant incision. Since the peritoneum in old people seems less capable of handling an infective insult than in the young, we have been guided by Blake's dictum "When in doubt—drain," even with the help of the antibiotics. In localized abscess, incision and drainage, preferably with local anesthesia, seemed sufficient.

In seven years our staff operated on only eight patients on the diagnosis of acute appendicitis. The diagnosis was correct in four instances and wrong in four. One additional case diagnosed as acute intestinal obstruction, proved to have a ruptured gangrenous appendicitis with peritonitis. Thus the diagnosis was accurate only four times in nine cases. Of the four cases incorrectly diagnosed as appendicitis, one had a massive perinephric abscess, one a perforated gangrenous diverticulitis of the sigmoid colon, one carcinoma of the cecum, perforated, with abscess, and one presumably a gastro-enteritis, since no pathology was found. The first two succumbed to sepsis. Of the latter two, one survived to die of already established metastases two months later and the other lived for three years, eventually to die of a cerebral-vascular accident.

Of the four cases correctly diagnosed and operated upon, three had already suffered perforation although their active symptoms were of but a day's duration or less. One patient with a four-day history of vague abdominal pain was found to have a well-developed abscess. This patient succumbed to peritonitis, as did the patient incorrectly diagnosed as intestinal obstruction. The other three survived. Mortality, 40 per cent.

# URGENT SURGERY IN AGED

TABLE III  
ACUTE APPENDICITIS  
Average Age 71

Preoperative Condition		Diagnosis		Postoperative Complications	
Arterio sclerosis	3	Correct	4	Peritonitis	2
Diabetes	1	Incorrect	1	Shock	1
A S H D	2	Operation		Cause of Death	
Nephritis	1	Incision and drainage of abscess	2	Peritonitis	2
Paralysis agitans	1	Appendectomy	2	(1 day and 9 days)	
Symptoms		Incorrect diagnosis	1	Result	
Pain	4	Anesthesia		Recovered	3
Vomiting	3	Ether	1	Died	2
Constipation	1	Cyclopropane	2	Mortality rate	40%
Fever	4	Cyclopropane and local	1		
Average Duration of Symptoms		Local and pentothal	1		
Days	2				

## ACUTE CHOLECYSTITIS

Infections and obstructions of the biliary tract presented some of the most difficult and dangerous problems found in the old age group. Of the patient of 70 or 80 with an acute cholecystitis or obstruction of the common duct, it may be assumed that cholecystitis has existed in chronic form for years and that the liver has suffered commensurate damage.

Our cases demanding urgent surgery for lesions of the biliary system numbered 34. Their average age was 73. Twenty-seven had advanced arteriosclerosis, while 19 had symptomatic arterio-sclerotic heart disease. Fourteen suffered from nephritis, three had suffered cerebral accidents, and three had had coronary occlusions. Three manifested chronic pyelonephritis, while among the other or associated disabilities were central nervous system lues, military tuberculosis, amyotrophic lateral sclerosis, diabetes and paralysis agitans.

Quigley,<sup>16</sup> reporting on biliary disease in patients who averaged 69 years of age, noted that his ward patients presented poorer surgical risks than did his private patients. He ascribed this difference to poorer economic status and earlier deterioration in the former, as well as to delayed hospitalization. Of his 100 patients, five were operated upon for acute cholecystitis and one survived.

The cases in our group rapidly became profoundly ill with the onset of acute gallbladder inflammation or with the sudden occlusion of the common duct. More than once we have been puzzled to differentiate between acute cholecystitis or biliary colic and a coronary infarction. The patients' condition deteriorated so rapidly as the result of infection, pain and dehydration that delay in undertaking operation greatly enhanced the risk. Jaundice was not well tolerated.

Fifteen patients in this group manifested jaundice as a result of occlusion of the common duct, and six of them had concurrent cholecystitis. Common

duct exploration and drainage alone was performed in two cases, and common duct drainage with cholecystostomy in three. All succumbed. Cholecystostomy alone was done three times for obstructive jaundice, with one survival. Cholecystgastrostomy for obstructing cancer was performed twice, with one death and one early survival. Common duct drainage with cholecystectomy was done five times, twice successfully. Thus, 11 of 15 patients presenting obstruction of the common duct with rapidly advancing jaundice were lost. Hemorrhage was not a factor in this mortality due, it is believed, to liberal administration of vitamin K.

Acute cholecystitis without evidence of common duct obstruction also progressed rapidly. Seven of 19 such cases were found to have perforated, four of them within 48 hours of the onset of the attack, indicating the need for early operation. The four cases of early perforation all died.

When confronted with acute cholecystitis in an old and enfeebled individual, it would seem to be good judgment to perform a simple cholecystostomy, preferably under local anesthesia. This policy was pursued with our patients at first. Of ten patients for whom cholecystostomies were performed, four recovered and six died. Two of the six deaths were due to peritonitis, which in both instances was found present at operation, due to perforation. (The other four deaths were ascribed to cerebral accidents, pneumonia and heart failure.) Later, influenced by the trend to cholecystectomy, we performed nine cholecystectomies for acute cholecystitis, with or without gangrene, and of these, five patients recovered and four died, two of peritonitis which was present at operation.

With cholecystectomy showing a 44 per cent mortality as against a 66 per cent mortality for cholecystostomy in old patients with acute cholecystitis, removal of the gallbladder would seem to be the operation of choice. But such a conclusion fails to take into account the patient's coincidental ailments. Where cholecystostomy was done, it was usually because the surgeon did not dare to do the preferred cholecystectomy because of the patient's condition. In both cholecystectomy and cholecystostomy, already established peritonitis accounted for roughly half of the deaths and removal of the gallbladder gave but little advantage in this one particular for which its added risk would seem to justify it as an emergency measure.

Of the total of 34 operated cases, 13 recovered and 21 died, giving a mortality rate of 62 per cent. Four deaths were due to peritonitis, six to pneumonia, six to cardiac decompensation or coronary infarction. There was one death each from cerebral accident, parotitis, multiple liver abscesses, gas bacillus septicemia and exacerbation of chronic osteomyelitis of the femur. The average length of survival of those who died was to the 25th postoperative day. It is assumed that the four surviving cases of carcinoma died later.

Delay in determining the cause of jaundice and reluctance to undertake surgical measures for its relief because of the grave risk involved has, we believe, worked to the disadvantage of some of our patients. It was difficult to decide when the time spent in preparation of the patient for operation began

to run against him in view of the rapidly increasing deleterious effects of jaundice and inflammation

TABLE IV  
ACUTE CHOLECYSTITIS AND COMMON DUCT OBSTRUCTION  
Cases 34      Average Age 73  
(Minimum 61      Maximum 91)

Preoperative Condition		Day of Operation		Cause of Death	
Arterio-sclerosis	27	Cholecystitis (av )	3	Peritonitis	4
A S H D	19	Obstructed duct (av )	10	Pneumonia	6
Diabetes	1	Anesthesia		Cardiac failure or coronary	6
Pyelonephritis	3			Cerebral accident	1
Nephritis	14	Cyclopropane	22	Other causes	
Cerebral accident	3	Local	11	Parotitis	1
Coronary accident	3	(Local with pentothal, 1)		Liver abscesses	1
Valvular H D	1	Ether	1	Gas bacillus septicemia	1
Tbc (miliary)	1			Septic fractured hip (pinned)	1
C N S Lues	1			(Late deaths carcinoma, 4)	
Amyotrophic lateral sclerosis	1				
Paralysis agitans	1			Death on postoperative day	
				(av )	25
Operative Condition				Result	
Cholecystitis	19			Recovered	13
(Perforated or gangrenous, 7)				Died	21
Obstructed common duct	15			Total mortality rate	62%
(6 with cholecystitis)				Cholecystitis	50%
Biliary carcinoma	5			Obstructed duct	73%
Biliary stone	10				

ACUTE INFECTIONS

Miscellaneous infections provided another group of emergencies requiring treatment regardless of the patient's age. Their management followed established principles of surgical procedure. Prompt and adequate drainage seemed to be even more urgent than in the younger age groups because of its rapidly damaging effect upon old and poorly vascularized tissues and because of poor systemic resistance.

The liberal and intensive use of the antibiotics in recent years has not succeeded in avoiding surgery for the control of local infective processes in these patients.

It was interesting to note the high incidence of septic arthritis occurring in this group. Apparently of hematogenous origin and without evidence of marked arthritis or of injury, this infection occurred nine times in our 36 cases. The shoulder joint was involved seven times, the hip once, and the elbow once. Ischio-rectal abscess occurred in eight cases. The other infections were scattered.

The physical status of the patients and the nature and severity of intercurrent disease were more important in their response to treatment and in the outcome than was age alone. The diabetics presented the most trying problems. Continuing or uncontrolled sepsis was the most common cause of death. The total mortality was 21 per cent.

TABLE V

## ACUTE INFECTIONS

Preoperative Condition		Cases	36	Average Age	73		
		Site of Infection		Anesthesia			
Arterio sclerosis	30	Septic arthritis	9	Vinethene	1		
Diabetes	6	Ischio rectal	8	Local	9		
Arterio sclerotic heart disease	15	Carbuncles	3	Pentothal	3		
Nephritis	9	(Neck—1)		Cyclopropane	19		
Coronary disease	1	(Back—2)		Ether	1		
Cerebral hemorrhage	2	Cellulitis	11				
Prostatism	2	(Toe — 2)		Postoperative Complications			
Paralysis agitans	2	(Finger — 2)		Pneumonia	2		
Pneumonia	2	(Hand — 2)		Sepsis	5		
Fractured femur	2	(Foot — 3)					
Cirrhosis	1	(Buttock — 1)		Cause of Death			
Decub tus	3	(Sacrum — 1)		Pneumonia	2		
Pyelonephritis	1	Empyema	2	Sepsis	5		
		Perinephric abscess	1				
		Ludwig's angina	1				
		Gangrenous ulcer	1	Day of Death			
		(Microaerophilic)		Operated Cases (av )	8		
		Operation		Results			
		Drainage	33	Recovered	26		
		No operation (died)	3	Died	7		
				Mortality rate (operated cases)	21%		

## SUMMARY

	Average Age	Number	Recovered	Died	Percent
Amputations	72	65	40	25	38
Obstructions	81	52	23	29	55
Appendicitis	71	5	3	2	40
Biliary	73	34	13	21	62
Infections	73	32	25	7	21
Total	74	188	104	84	44

## CONCLUSIONS

1 Among old people suffering from chronic or degenerative disease, there occasionally occur surgical emergencies which urgently require operation to save life

2 One hundred eighty-eight indigent patients of average age 74 were operated upon for surgical emergencies at the Goldwater Memorial Hospital in a seven-year period. These conditions consisted of gangrene of the extremities, intestinal obstructions, inflammations and obstructions of the biliary system, appendicitis, and various infections

3 Such conditions often presented difficulties of diagnosis which delayed their recognition

4 These patients presented poor operative risks and required maximum preoperative supportive and preparatory treatment. Such measures could not always be pursued to the desired extent without unduly delaying surgical relief

5 Operations were designed to meet the emergency with the least injury and shock to the patient

6 General anesthesia, properly chosen and administered, was well tolerated by such patients

7 The postoperative period required attentive nursing and supportive and protective measures, including transfusions, the antibiotics, adequate alimentation, and minimum confinement to bed

8 The mortality rate was 44 per cent The preexisting ailments of the patients were the greatest factor in this mortality

9 Pneumonia was the major cause of death (34 per cent of deaths) Forty-nine per cent of the pulmonary complications began ten days or more after operation

10 Complications not directly attributable to the operation or to the emergency for which it was performed, accounted for about half of the deaths

11 Prompt treatment may save well over half of the victims of acute surgical emergencies in old and chronically ill people

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DISCUSSION —DR FREDERIC W BANCROFT, New York I have had the opportunity to read Doctor Cutler's report in full and in many ways I am sorry that he has had to cut the contents of this report in order to stay within the time limit allowed for reading the paper

In 1930, of a total population of 123 million, 14 million reached the ages of 50 to 64, and 6,600,000 were 65 or over It has been estimated that by 1980 we will have 25 million people over 65 years of age \*



It is obvious that we must realize the importance of surgery in the older age groups. I agree with Doctor Cutler that in the older age groups, after affecting hydration and with the necessary blood for replacement at hand, delay for refinements in diagnosis may lose a patient. Immediate surgery is often the *sine qua non*. Also, I agree with him that early mobilization is particularly urgent in the aged. Twenty years ago while at the Lincoln Hospital, I got older people out of bed on their fourth or fifth postoperative day in order to decrease the incidence of pulmonary complications.

In the short time given to me, I am going to confine most of my remarks to mid-thigh amputations. My experience at the City Hospital makes me disagree with Doctor Cutler in the type of mid-thigh amputation he advocates. Our mortality in diabetic and arteriosclerotic gangrene with muscle-cut amputations was distressing. We were using the mid-thigh muscle flap technic. At the same time, I was impressed with the better results being obtained at the Veterans Hospital in the same type of case by a modification of the Callander operation as devised by Dr. Allen Fuller, Chief Surgeon at the Veterans Hospital.

As this amputation embodies certain fundamental surgical principles, I should like to describe briefly his operation. A circular incision is made just distal to the patella. Immediately towel clamps are applied to the skin and deep fascia as the incision is made around the entire circumference. This procedure prevents the separation of the delicate areolar tissue which connects skin and fascia and protects the circulation of both. These clamps are kept on during the entire operation. After the external hamstrings are severed, a finger is passed between the popliteal vessels and the posterior surface of the knee joint. A tape is passed blindly around these vessels and securely tied. The patella is excised and the femur is hugged closely, pushing the muscles upward until they have been separated for a distance of six or eight inches above the condyles. The femur is then sawed through with a Gigli saw and the leg is removed. Then the muscles with the attached skin and fascia are allowed to drop over the end of the femur, the tape is removed and individual vessels are separately tied and the sciatic nerve is appropriately treated. The fascia and skin may then be united without tension.

Tables I and II show the decrease in mortality at the City Hospital and at the Veterans Hospital with this type of procedure.

TABLE I  
AMPUTATIONS ABOVE THE KNEE

<i>City Hospital</i>	<i>Amputations</i>	<i>Deaths</i>	<i>Mortality Percentage</i>
Previous to 1937	57	31	54.4
1938-1941	63	39	62
Sleeve amputations	13	4	33.4
Sleeve amputations plus refrigeration	13	2	15.4
<i>Veterans Hospital</i>			
Sleeve amputations	33	8	24

TABLE II  
MORTALITY—VETERANS HOSPITAL

<i>Total 103 Cases</i>		<i>Days 1-10</i>	<i>10-30</i>	<i>Over 30</i>	<i>Total Per Cent</i>
Below Knee	60	10%	4%	0%	14%
Knee	33	18%	3%	3%	24%
Mid Thigh	10	10%	0%	20%	30%
Mortality rate, 103 cases — 19 deaths — 18%					
Average age all patients				50	
Average age all deaths				59	

Tables I and II show the decrease in mortality with the Fuller type of sleeve amputation at the lower thigh

If time permits, I should like to state briefly some work that has been done by Ned Schnayerson at Welfare Island to decrease the number of amputations in the older age group. He has taken arteriograms of people with intermittent claudication and found that often there are blocked segments of the femoral or popliteal arteries. He considers these blocked segments to act as nerve stimuli creating venospasm. By excising these segments and being careful not to interfere with the collateral circulation, he has had some astonishing results. One patient who could walk only two blocks is now walking eight miles. Minor amputations have been done with satisfactory healing.

DR CONDUCT W CUTLER, JR, New York (closing). I am very much indebted to Doctor Bancroft for his discussion. He understands our problems so well, having worked in the same general line for many years, and recognizes the difficulties that confront us in aged patients. The observations he has made concerning amputations I think are particularly helpful, and we should be encouraged toward less radicalism if it were not for two facts: the vessels and tissues in the lower third of the thigh, especially where diabetes is present, are likely to be already involved in the sepsis, and in arteriosclerosis, where the vessels are already occluded at that level, one may not do an amputation with the hope of securing adequate circulation in the stump. We have done the Callander amputation and also the sleeve-type modification. Of four cases one required reamputation because of sepsis. Two were done below the knee and one developed gas infection and required reamputation. Fifty-six guillotine amputations were done. In 46 there was suture of the muscles and skin, 30 suppurated, 2 with gas infection. In 16 the skin alone was sutured and six suppurated. That discouraged us from thinking we could safely perform either flap or Callander operations in the septic cases.

Our patients requiring emergency amputation averaged 72 years of age. In the 25 who died, four died of conditions directly attributable to operation, three of shock, one of sepsis. The others died for the most part of pneumonia or from unrelated causes which resulted in death up to a month after operation.

In this report we have not attempted to adjust the mortality figures in our favor. It must be recognized that a good many patients would not have died had they not required operation, and it seemed unfair to excuse the deaths on the basis of pre-existing disease. So we have accepted responsibility for the deaths as long as the patients were in the hospital and under our care. We hope to be able to do better, but I think it is right to face the issue squarely and recognize that in the chronically ill aged patient, particularly in surgical emergencies, we do have a problem of considerable and increasing magnitude.

# EXPERIENCES IN THE SURGICAL TREATMENT OF MULTIPLE VISCERAL NEOPLASMS\*†

ALEXANDER BRUNSCHWIG, M D,\*\* AND PAUL W SCHAFER, M D ‡

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THE OCCURRENCE OF MULTIPLE VISCERAL NEOPLASMS is of interest because of the implications in regard to etiology. Several collective reviews have appeared in the literature in recent years<sup>1-6</sup> based for the most part upon necropsy findings. In view of the increased efficiency in the surgical treatment of neoplasms which has resulted in a greater incidence of prolonged survival following the treatment of one growth, the question of multiple neoplasms occurring simultaneously or developing successively assumes added clinical importance.

The following discussion is based upon a clinical experience with nine patients presenting multiple symptom producing visceral neoplasms. They have been classified into three groups. A. Those with multiple tumors closely situated to one another and producing symptoms clinically accountable by one growth. In these patients the multiplicity of the growths was discovered only at operation or upon study of the pathologic specimens. B. Those with two tumors rather widely separated and manifesting simultaneously the symptomatology of two separate growths. C. Those in whom one growth was excised to be followed later by the development of a second independent growth, which in turn was also resected.

## CASE REPORTS

### Group A

**Case 1 (Fig 1A)**—F O, male, 59 years old, admitted June 27, 1945, complaining of epigastric pain aggravated by eating, and vomiting, three months, loss of 15 pounds weight during the same period. Roentgenograms revealed "an obstructing lesion in the pylorus, 3 to 4 cm proximal to the duodenal bulb." Gastroscopic examination revealed an ulcerating polypoid mass as far as the angulus—impression, carcinoma.

On July 3, 1945, laparotomy was performed and a typical carcinomatous process discovered in the lower stomach. Palpation of the first segment of duodenum revealed a small rounded boggy mass that seemed to extend backward into the stomach. Radical gastrectomy including the first segment of duodenum was carried out and a Polya type of gastrojejunostomy performed.

Study of the opened stomach showed a flat carcinomatous ulcer 5 cm in diameter in the pre-pyloric region, beyond this was a yellowish rounded mass 1.5 cm in diameter attached by a narrow base to the mucosa just proximal to the sphincter. The most protruding portion of the mass projected through the sphincter itself into the first segment of duodenum. This was obviously a pedunculated lipoma producing a ball-valve stoppage at the pylorus. Histologic examination confirmed the carcinomatous nature of the former

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lesion and the fact that the latter growth was a lipoma One year and six months after operation, the patient remains well (Case previously cited)

**Case 2 (Fig 1B)**—F Z, white male, age 46, admitted January 29, 1945, complaining of vomiting of "heavy foods" during previous five weeks, epigastric "fullness" for seven weeks and 25 pounds loss in weight for six months Roentgenographic examination of the stomach revealed "ulcerating polypoid neoplasm of the gastric antrum"

Celiotomy was performed Feb 5, 1945, at which time what appeared to be a large infiltrating carcinoma was encountered in the pylorus with infiltration into the transverse

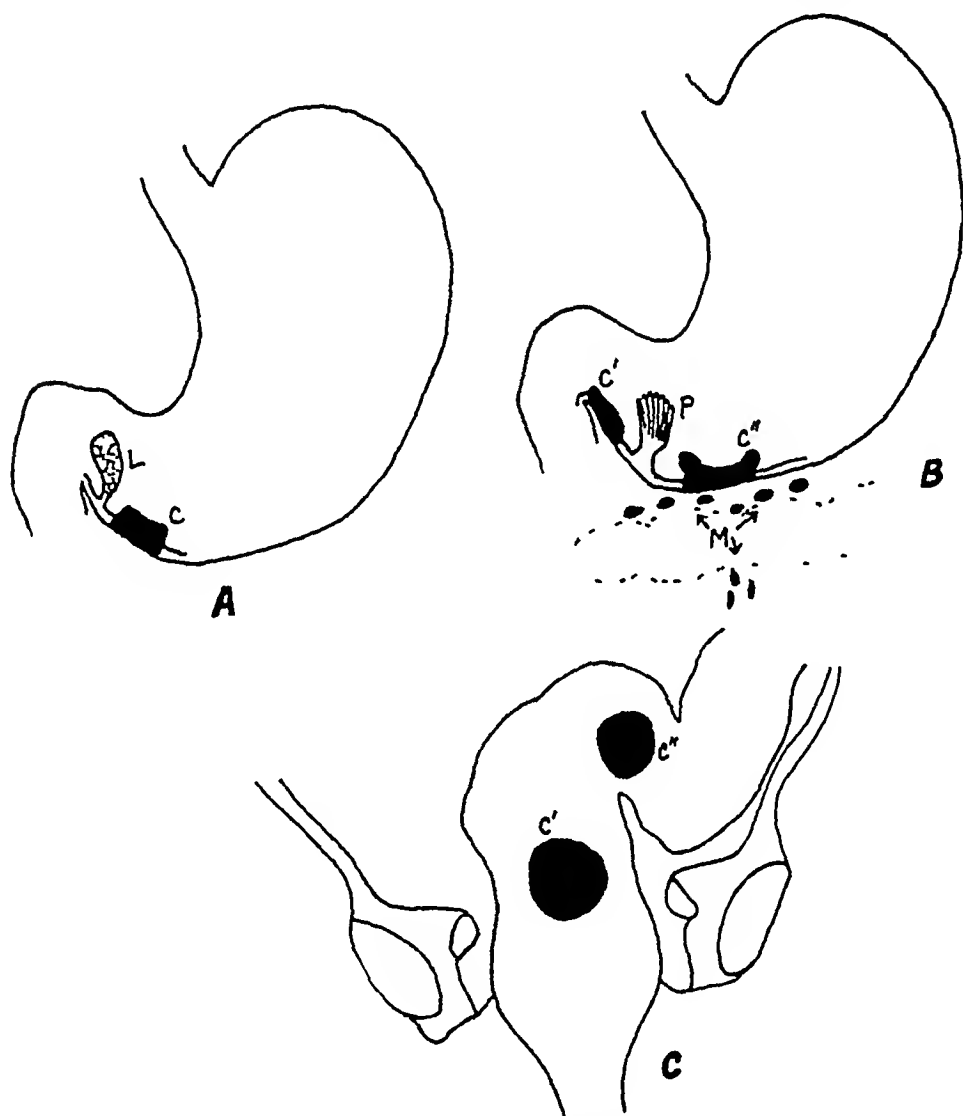


FIG 1—Diagrams of multiple visceral neoplasms manifesting themselves clinically as one growth

A Case 1 L, pedunculated lipoma in pylorus, C, carcinoma in prepyloric region The former might well have produced obstructive symptoms

B Case 2 C', scirrhous carcinoma in pylorus, P, papilloma in prepyloric region, C'', ulcerating carcinoma proximal to the latter M, metastases in transverse meso-colon and about the superior mesenteric vessels

C Case 3 C' and C'', two separate primary carcinomas in pelvic colon Patient 83 years of age at time of successful resection

meso-colon almost to the colon itself and with metastases to lymph nodes about the superior mesenteric vessels A radical gastrectomy with resection of most of the transverse colon and its mesentery together with the metastatic nodes about the superior mesenteric vessels was carried out Followed by gastro-jejunostomy and double barrel colostomy The latter was closed four weeks later

Study of the surgical specimen (stomach) when opened revealed three separate neoplasms along the greater curvature (Fig 2). The first, a scirrhus carcinoma presented as a flat ulceration 2.5 cm in diameter just proximal to the pyloric sphincter. Two cm proximal to this was a benign papilloma with small base. The lesion measured 3.5 cm in greatest diameter. Separated from the base of the papilloma by 5 cm of normal mucosa was a second carcinomatous ulcer with raised rolled edges measuring 6.5 cm in diameter. There were many metastatic nodes. The patient did well and



FIG 2—Photograph of surgical specimen consisting of opened resected lower three-fourths of stomach exhibiting three separate neoplasms. C, scirrhus carcinoma in pylorus, P, pedunculated papilloma, U, ulcerating carcinoma. Study of the specimen revealed small areas of normal uninvolved gastric wall between each of these lesions. N, portion of metastatic nodes removed from about the superior mesenteric vessels. The transverse colon and meso-colon were also resected because of secondary involvement but are not shown in the photograph. The patient lived for one year to receive palliation for most of this period.

returned to work for several months. However, in Dec 1945, there was severe back pain and dyspepsia. He was finally readmitted to the hospital and died Jan 27, 1946, necropsy revealing carcinomatosis.

**Case 3 (Fig 1C)**—J. F., white male, 83 years of age, admitted Aug 10, 1945, complaining of severe constipation and tarry stools for one year, bleeding from rectum and pain in the rectum for six months. On rectal examination a polypoid carcinomatous mass was palpated at the tip of the finger.

Celiotomy was performed on Aug 18, 1945, because no metastases were palpated,

a typical combined abdomino-perineal resection was performed. Study of the 30 cm of lower colon removed showed two separate raised, circular ulcerating carcinomas, one 8 cm above the anus and one 6 cm above the first growth. The lower one measured 3 cm in diameter, the upper one 6 cm in diameter. Sections showed metastases in one of eight lymph nodes examined.

Sept 1947, two years and one month after operation, the patient is well and normally active.

#### Group B

**Case 4.** (Fig 3A)—F N, male, 58 years, admitted May 25, 1946, complaining of difficulty in swallowing, especially solid foods, for the past three months, loss of 15 pounds in weight during the previous four months, "gas on stomach" following ingestion

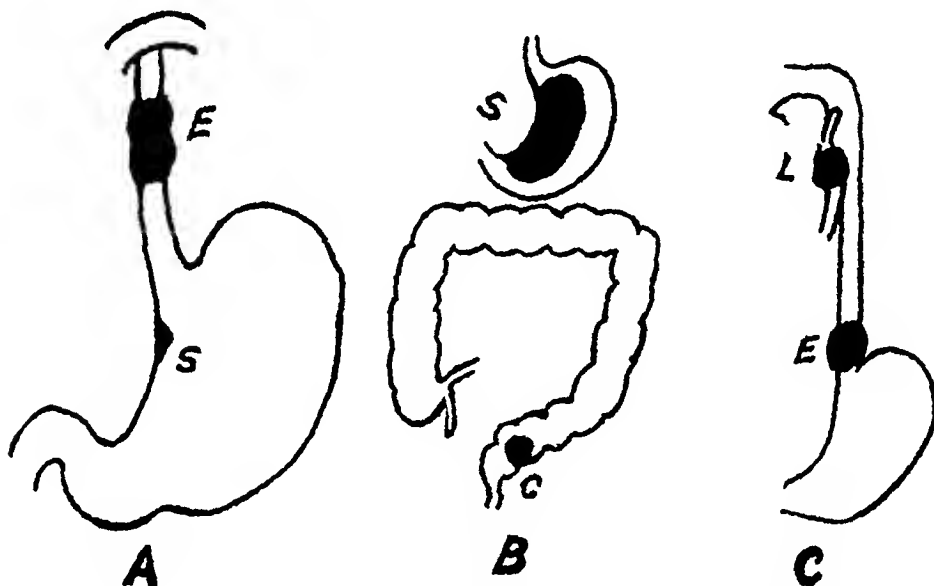


FIG 3—Diagrams of multiple visceral neoplasms manifesting themselves simultaneously as two separate growths

A Case 4 E, carcinoma of lower third of esophagus and S, carcinoma on lesser curvature of the stomach

B Case 5 S, carcinoma involving the major portion of the stomach C, carcinoma of the pelvic colon

C Case 6 L, carcinoma of the larynx, E, carcinoma at the cardio-esophageal junction

of certain foods, for the past one and one-half years. Roentgenographic examination revealed a small partially obstructing neoplasm in the lower esophagus.

On May 31, 1946, a left thoracotomy was performed removing the 8th rib. A carcinoma was found in the mid-portion of the lower half of the esophagus measuring about 8 cm in length. When the diaphragm was incised for mobilization of the stomach and the latter brought upward a small firm lesion was discovered on the lesser curvature. The stomach was opened and the latter observed to be a sharply penetrating ulceration. It was excised by elliptical incisions and the stomach repaired. The lower 2/5 of the esophagus and upper fourth of the stomach were then resected, the stomach closed and brought upward for esophago-gastrostomy by the usual method.

Histologic study revealed the esophageal lesion to be a squamous cell carcinoma. Sections of the gastric lesion revealed it to be an adenocarcinoma. Sections of the small mass from the liver revealed it to be a focus of necrosis with inflammatory reaction. No evidence of neoplasm was here observed.

Convalescence was uneventful and he was discharged on the 12th day postoperative.

**Case 5 (Fig 3B)**—M W, white male 62 years of age, admitted April 24, 1945, complaining of loss of 10 or 15 pounds in weight during the previous three months, increasing constipation for the past three years, and a feeling of fullness in the epigastrium of 4-5 months duration. Roentgenographic examination of the stomach revealed "one and possibly two ulcers almost certainly due to neoplastic involvement." Proctoscopic examination revealed an ulcerating polypoid carcinoma at 10 cm distance.

On April 28, 1945, an upper abdominal laparotomy was performed and a large tumor mass involving almost the entire lesser curvature of the stomach was found, palpation in the pelvis revealed a firm neoplastic mass in the rectal colon below the peritoneal reflection. No lymph node or hepatic metastases were found in the upper or lower abdomen. A total gastrectomy was performed. Histologic study confirmed the presence of adenocarcinoma. Following satisfactory recovery from this procedure, a one stage combined abdominoperineal resection was carried out on May 24, 1945, with removal of the terminal 24 cm of colon. In the lower portion an oval carcinoma 3 x 2 cm was present. Histologic study confirmed the diagnosis of adenocarcinoma and sections from three lymph nodes failed to reveal metastases. Convalescence was again satisfactory except for symptoms of prostatism. On June 22, 1945, a transurethral electro-resection was done by Dr W W Scott. He was finally discharged on July 14, 1945. In January, 1947, one year and nine months after operation, the patient is well and normally active, but there is a small fistula at the site of the perineal wound (no evidence of recurrences). The appetite is good.

**Case 6 (Fig 3C)**—N I, Japanese male, 63 years of age. In June, 1946, the patient experienced epigastric pain related to the swallowing of solid foods and later induced even by the swallowing of soft foods. There was also hoarseness said to exist for "three or four years." Laryngoscopic examination in August, 1946, revealed a carcinoma of the right true vocal cord. Histologic study of a biopsy confirmed the diagnosis. He received irradiation therapy to the larynx at the Chicago Tumor Institute under direction of Dr Max Cutler. The laryngeal neoplasm subsequently resorbed completely. On Oct 2, 1946, he was admitted to the University of Chicago Clinics where roentgenographic studies revealed a lesion typical of carcinoma at the cardioesophageal junction.

On Oct 8, 1946, a left transthoracic cardioesophagectomy was performed removing the lower third of the esophagus and upper fourth of the stomach together with the contiguous portions of the diaphragm because of invasion by tumor. The stomach was brought upward into the mediastinum and esophago-gastrostomy performed. The immediate postoperative condition was satisfactory but the patient expired suddenly on the afternoon of the third day. Necropsy revealed no adequate explanation for death. There was no hemorrhage, nor evidence of infection. Histologic study of the laryngeal biopsy and of the lower esophageal growth showed both to be squamous cell carcinomas but of different histologic types.

#### Group C

**Case 7 (Fig 4A)**—A G, white female, age 52. Two years previously a carcinoma of the sigmoid had been resected by the "Mikulicz procedure" in another institution. The histologic diagnosis was confirmed. Admitted Oct 20, 1937, complaining of "several severe hemorrhages from the bowel." A barium enema revealed a large spherical smoothly outlined filling defect in the right portion of transverse colon just distal to the hepatic flexure.

On Oct 25, 1937, laparotomy was performed and the lesion observed through the stretched but intact colon wall. It was obviously a lipoma 6 cm in diameter. The involved segment of colon bearing the tumor was exteriorized, cut away, and the resultant double barrel colostomy subsequently closed. During the operation exploration of the liver, upper and lower abdomen failed to reveal evidences of metastases.

The patient remains well ten years later.

# MULTIPLE VISCERAL NEOPLASMS

**Case 8.** (Fig 4B)—M B, white female, 54 years of age, admitted complaining of dull epigastric pain, non-radiating, intermittent and associated with rumbling sounds in the abdomen. There had been alternating liquid and formed stools—duration of complaints, "over two months." Barium enema revealed an annular constricting lesion in the cecum.

On Dec 2, 1940, a right hemicolectomy with ileo-transverse colostomy was performed. Convalescence was uneventful for 18 days when a deep right flank abscess was discovered and drained and a week later she was discharged.

Study of the surgical specimen which consisted of the right half of the colon revealed

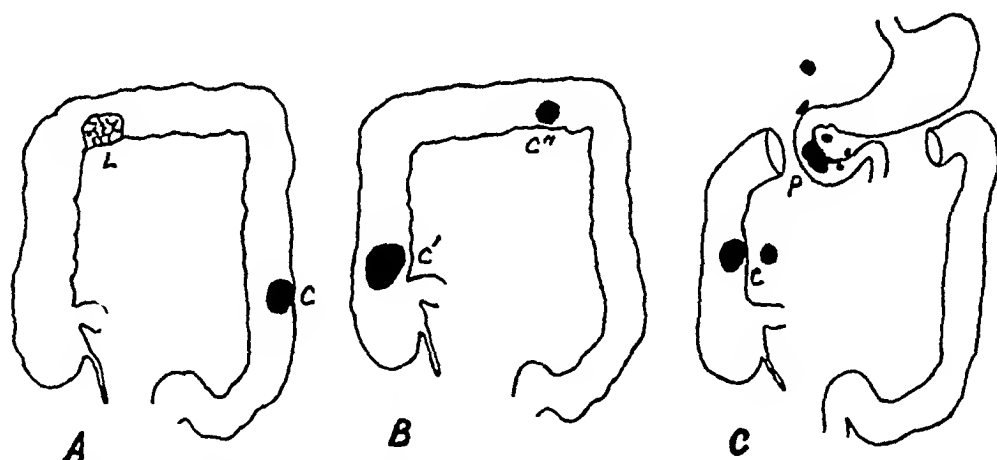


FIG 4—Diagrams of multiple carcinomas or benign tumor occurring successively and successfully resected

A Case 7 C, carcinoma of descending colon resected in 1935, L, large pedunculated lipoma causing hemorrhage and partial obstruction resected in 1937. Patient well in 1947.

B Case 8 C', carcinoma of ascending colon resected in 1940. Well until 1946 when because of obstruction was re-operated upon and found to have what was apparently another primary growth near splenic flexure C'', and also liver metastases. Jan 1947, alive but has deteriorated due to advancing carcinoma.

C Case 9 P, large carcinoma of papilla of Vater with regional lymph node metastases resected in May, 1943. C, carcinoma of ascending colon with regional lymph node metastases resected in November, 1945. March, 1947, patient well and returned to usual occupation.

an annular carcinoma 4 cm in width in the cecum. Histologic study showed metastases in two of 13 nodes examined.

The general condition remained satisfactory until Aug 9, 1946, at which time she was admitted to the Woodlawn Hospital (Chicago) under the care of Dr H P Jenkins, complaining of abdominal pain, nausea and vomiting of five days duration. Barium enema revealed some evidence of constriction in the colon near the splenic flexure. The abdomen was decompressed with the Miller-Abbott tube and the patient discharged. She was readmitted as above on Sept 8, 1946, after repeated attacks of obstruction at home.

Celiotomy was performed (Doctor Jenkins) on Sept 12, 1946. Many adhesions were encountered, a tumor mass was palpated in the transverse colon near the splenic flexure. There were numerous metastases throughout both lobes of the liver. The area of the ileo-transverse colostomy was identified. The remaining portion of transverse colon bearing tumor was exteriorized and later resected with closure of the colostomy. She was discharged with colostomy closed.

Pathologic study of the specimen showed a primary carcinoma in the left portion of the transverse colon a short distance proximal to the splenic flexure.

**Case 9** (Fig 4C)—N G, white male, age 53, admitted April 4, 1943 complaining of icterus of varying severity, two months duration, and constipation, noticeably aggra-



vated in the previous eight months. Roentgenographic examination showed a papillomatous growth in the region of the papilla of Vater. On May 17, 1943, a one-stage pancreatoduodenectomy was performed for excision of a large papillary carcinoma of the ampulla with regional lymph node metastases. One metastatic node was high in the porta hepatis over the junction of cystic duct with common duct. Convalescence was satisfactory and following discharge he returned to work.

By November, 1945, there was again loss in weight and discomfort in the right abdomen. A questionable mass was palpated deep in the right flank. In February, 1946, this finding had become definite and he was readmitted to the hospital where another laparotomy was performed on March 6, 1946. The upper abdomen and liver exhibited no metastases. A cirrhosis of the liver noted at the first operation was now seen to be more pronounced. In the mid-portion of the ascending colon there was a papillary carcinoma about 4 cm in diameter with obvious lymph node metastasis in the corresponding mesentery. A right hemicolectomy was uneventful and the patient returned to his usual occupation. He is well one year and six months after the second operation and 4 years and 6 months after the initial operation.

#### DISCUSSION

The colon is a relatively common site for multiple malignant tumors in the abdominal viscera. In a review of 726 histologically verified cases from the University of Rochester, N. Y., series Mider found 21 instances of multiple malignant growths in the colon. There were four instances in which the neoplasms manifested themselves successively, two died, and two survived. One of the latter presented a neoplasm at the splenic flexure in 1938, and in 1942 had carcinomas in the rectum and descending colon respectively. He remains well three years after the last operation. The other patient, a female, presented a carcinoma of the cecum in 1928 and one in the transverse colon in 1929. She is apparently well 16 years later, after resection.

There were nine cases of multiple malignant neoplasms present synchronously in the colon and surviving eight to 78 months after resection.

Slaughter, in an excellent collective review of the whole subject of multiplicity of origin of malignant tumors, also noted that, with the exception of the skin, the colon was by far the most frequently involved of all the organs.

In the series reported above, the stomach was the site of multiple neoplasms in two instances, the colon in three instances, the larynx and esophagus in one instance, the esophagus and stomach in one instance, the stomach and colon in one instance, the papilla of Vater and colon in one instance. All lesions were not malignant. In two instances one of the stomach was benign and in one instance one of the colon lesions was benign, but in two of these the benign lesions produced symptoms.

The classical teaching is to ascribe as often as possible, all symptomatology to one pathologic process. In the case of neoplasms, especially malignant, recurrence of symptomatology in the great majority of instances is due to recurrence of the neoplasm and/or its metastases. However, sufficient data has now been published to indicate that the multiplicity of neoplasms producing symptoms synchronously or successively as they develop, is not an extreme rarity and in the follow-up of patients having had one neoplasm resected this possibility is to be borne in mind.

SUMMARY

The case histories of nine patients are reviewed in which there was multiplicity of malignant or benign symptom producing neoplasms of various viscera. The details of management are discussed.

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# RESECTION AND PRIMARY ANASTOMOSIS IN THE TREATMENT OF GANGRENOUS OR NON-REDUCIBLE INTUSSUSCEPTIONS IN CHILDREN\*

## A Safe, Simple, One-Layer Silk Anastomosis

CLARENCE DENNIS, M D

FROM THE DEPARTMENT OF SURGERY UNIVERSITY OF MINNESOTA HOSPITALS SUPPORTED BY A RESEARCH GRANT FROM THE GRADUATE SCHOOL OF THE UNIVERSITY OF MINNESOTA

A REVIEW OF THE LITERATURE on the management of recurring, irreducible, and gangrenous intussusceptions offers little evidence of a satisfactory solution of the problem. Wangensteen's review indicates that to the time of publication (1942) no series of cases of resection had been reported without very high mortality. Other methods have also been employed, such as the short-circuiting procedures of Rutherford and of Montgomery, or the cutting of the intussusciens by Brown, but most authors seem to favor exteriorization. Of primary anastomoses, the case of Dowd is among the earliest successes, but the experience of Perrin and Lindsay with nine survivors in 29 attempts and of Hipsley with none surviving is more usual.

Success in a case of gangrenous intussusception in 1940 prompted the author to employ resection and primary anastomosis routinely for strangulating obstructions. Success in other types of cases led to confidence in application of the method to more intussusception cases. At the University of Minnesota Hospitals, intussusceptions rarely arrive in the first 24 hours, and the experience therefore has been that almost 50 percent of these cases have required resection between November 1940 and March 1, 1947.

### CASES TREATED

**Case 1**—U H #702210, male, age 39 days, was admitted November 20, 1940, in a dehydrated state with a 60-hour history and findings typical of intussusception. The abdomen was tympanitic and distended. He was transfused and given 100 cc of 0.9 per cent NaCl solution before operation, and was slowly transfused during operation, which was done under open ether. Through a right lower rectus incision, an ileocolic intussusception was identified, and the apex was milked back into the ileum, but the lesion could not be completely reduced despite considerable manipulation, efforts were terminated by occurrence of a serosal tear. The upper margin of the intussusciens was observed at this point to be discolored, edematous, and firmly sealed to the bowel above. Exteriorization was considered at this point, but the mesoileum was not long enough to permit it. The involved area was therefore resected from a point 2 cm above the ileocecal junction to a site 5 cm above the upper margin of the intussusciens and an aseptic, end-to-end anastomosis of the Martzloff-Burget type was performed with catgut used for the internal layer. About one gram of sulfanilamide was implanted, partly about the anastomosis and partly in the wound, during catgut closure.

After operation the patient was given 100 per cent oxygen, nasal gastric suction, and intravenous sulfathiazole for 36 hours. Feces were passed at 48 hours and the

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\* Read before the Meeting of the American Surgical Association, March 25-27, 1947, Hot Springs, Va.

temperature reached normal at 72 hours. Early feeding was cautious, but the patient improved rapidly. Dismissal was delayed until 22 days postoperatively by late development of bronchopneumonia. He was last seen four months later, and seemed a normal baby at that time.

The specimen presented areas of necrosis, and there was hemorrhagic infiltration of the gut wall.

**Case 2**—U H #703673, female, age four months, was admitted January 20, 1941, with a 21-hour history and findings typical of intussusception. After hydration, transfusion, and ether anesthesia, the intussusceptum was found to have progressed into the descending colon, the base of the cecum not being inverted. It was manipulated back into the terminal ileum, here a necrotic area came into view, and perforation occurred. The mesentery being long, the area was exteriorized over a glass rod, using silk abdominal closure. The double-barreled ileostomy was opened in two days, but the baby had a bout of partial obstruction and fever which lasted five days. Thereafter, she gradually lost weight and strength despite forced feedings and free drainage from the ileostomy. After vigorous intravenous preparation, the ileostomy was closed, using a Martzloff-Burget anastomosis, on February 24th, with implantation of a gram of sulfanilamide. She again had prolonged postoperative ileus and fever, and did not pass stool until five days later. Following a bout of pneumonia, she finally recovered, and was dismissed 61 days after admission.

She was last seen a month later at which time she was considered normal.

Following the rather precarious course of this patient, it was decided to employ primary closed anastomosis on these cases in the future.

**Case 3**—U H #714167, male, age 11 months, was admitted October 31, 1941, with a 40-hour history. After preparation, laparotomy under open ether permitted reduction of the apex from the hepatic flexure to a point 25 cm above the ileo-cecal junction. Here necrotic bowel prompted resection without complete reduction. Thirty centimeters was resected, and a Martzloff-Burget anastomosis was made using catgut for the inner layer, with dusting of 2 Gm of sulfathiazole about the anastomosis\*. Although old blood was passed by rectum within a day, removal of gastric suction was not tolerated until one week after surgery. Dismissed at 26 days, delayed by abscess at site of venesection.

The patient was last seen six weeks later, and was well.

The specimen showed widespread infarction of bowel.

**Case 4**—U H #729600, male, age 9 years, was admitted March 9, 1943, with a history of blood in the stool at intervals, with cramps, for several months. Acute onset of severe intermittent cramps began 28 hours before surgery. Study showed high small bowel obstruction. Exploration through a right rectus incision under cyclopropane anesthesia revealed a massive high ileo-ileac intussusception with massive adhesions of the margin of the intussusciens to the base of the cecum. Following considerable reduction, manipulation was halted by an irreducible portion containing a mass, and by perforation. Sixty centimeters of ileum was resected, and Martzloff-Burget anastomosis with catgut for the inner row was made, implanting about 50 mg of sulfanilamide between rows, but not elsewhere. Appendectomy. Postoperative course uneventful, with removal of suction in four days. Total hospitalization 11 days.

The patient is in good health at the present time, without anemia or abdominal complaints.

The specimen showed a polyp 6 x 4 cm with a stalk 2 cm in diameter, which served as the apex of the intussusciens.

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\* Procedure by L. J. Hay, then resident on Surgery and now National Cancer Fellow at the University of Minnesota.

**Case 5**—U H #737486, male, age 43 months, was admitted November 17, 1943, with a history of three days of nausea and vomiting and two days of severe cramps coming every 20 to 30 minutes without blood in the stool. Films showed gas in the cecum, and an erroneous diagnosis of colo-colic intussusception was made. Exploration under cyclopropane anesthesia showed a mass near the cecum, which reduced easily before it could be delivered, the terminal ileum remained edematous, and the junction wide open so that a finger could palpate the lumen of the ileum by inversion of the cecal wall. Several sessile polypoid masses could be felt by this procedure in the last three centimeters of ileum.

Five days later, after a smooth course to that time, he developed severe cramps more typical of ileac intussusception in that they came every three to five minutes. Re-exploration through a separate incision. Ileo-colic intussusception was easily reduced, and the same masses were palpated inside the thickened terminal ileum. In the belief they had played a part in the development of intussusception, the last 11 cm of ileum was resected. Ileocecal junction closed with silk, and end-to-side anastomosis of ileum to ascending colon easily made by Martzloff-Burget plan. Appendectomy. Silk closure.

Postoperative course uneventful. Suction six days. Total stay 24 days. Patient checked and well at six weeks.

The specimen showed a polypoid hyperplasia of a Peyer's patch about 3 centimeters from the ileocecal junction.

**Case 6**—U H #721360, male, age 24 months, was admitted May 20, 1944, with typical findings and a 30-hour story. Under cyclopropane anesthesia, the apex of an ileocolic intussusception was milked, with considerable manipulation, into the terminal ileum. When complete reduction had been accomplished, an area of necrosis with hemorrhagic infarction dictated resection of a 15 cm segment some 9 cm above the ileocecal junction. Oblique, aseptic, end-to-end anastomosis with 180 degree rotation was used because of the very small diameter of the bowel (1 cm). A few mg of sulfanilamide was implanted between rows, and in closure of abdomen with silk.

Postoperative course uneventful. Suction three days, full diet at five days, and home in ten days.

The specimen showed extensive gangrene.

**Case 7**—U H #746278, female, age seven and one-half months, was admitted July 29, 1944, with a history of intermittent pain, vomiting, bloody stool beginning five days earlier and lasting only 12 hours. Thereafter she had taken feedings and had normal stools. A day later developed fever, anorexia, and then vomiting. Admitted with temperature 104, Hgb 5.1 Gm per cent, pus and casts in urine, and negative abdomen. After admission she developed severe distention, surgical consultation eight days after onset of trouble.

Patient was explored under cyclopropane anesthesia with diagnosis definite only as to high small bowel obstruction. Hugely distended ileum precluded exploration until aseptic decompression, removing 200 cc gas and 200 cc feces.<sup>19</sup> An ileocolic intussusception was reduced easily. A second intussusception was found 25 cm higher. After reduction, a Meckel's diverticulum was found at the apex. It was observed a few minutes because of doubtful viability, during this time redevelopment of intussusception at the area was seen to be occurring. This area was resected and an aseptic, oblique, end-to-end anastomosis with 180° rotation was made, with 20 mg sulfanilamide between rows. Silk closure.

Postoperative course was complicated by separation of a portion of the wound at six days, with extrusion of a tag of omentum, and drainage. Treated conservatively with taping because of fear of peritoneal infection. Suction out at six days. Course also complicated by poor renal function, the blood urea nitrogen level reaching 105 mg per cent at five days. This gradually improved on withdrawal of sulfadiazine. There was some

abdominal distention at intervals, but she gained weight and strength. Hospitalization was prolonged for mandelic acid therapy of the urinary infection. Total stay 78 days.

The patient returned for hernia repair June 13, 1945, weighing 11.6 kg (18 mo). Discharged in apparently excellent condition thereafter.

**Case 8**—U. H. #772340, male, age five and one-half months, was admitted October 27, 1946, with a four-day story and physical findings classical for intussusception. Very lethargic and dehydrated. After hydration and transfusion, the abdomen was opened through a right lower quadrant oblique incision under local and cyclopropane anesthesia. The right colon contained intussusceptum, the base of the cecum and appendix being involved, and manipulation failed completely. A right hemi-colectomy was therefore performed, with surprisingly little difficulty, and a single-layer closed silk end-to-end anastomosis was made between the ileum and the transverse colon. Gaseous distention of the small bowel was relieved by aspiration of 160 cc. of air with silk inversion of the puncture site, following which silk closure was easily accomplished.

The postoperative course was smooth. Fever disappeared and feedings were easily started the same day the nasal gastric tube was removed, 48 hours after surgery. The total hospital stay was 11 days.

Patient was last seen a month later and was doing nicely at that time except for occasional stools softer than normal.

The specimen showed the apex of the intussusceptum to be the base of the cecum, which was gangrenous\*.

#### THE CHOICE OF PROCEDURE

Cases requiring resection may at the present time be managed either by exteriorization or by resection and primary anastomosis. In their book, Ladd and Gross favor exteriorization and report seven recoveries in 25 cases. Gross is preparing a report at the present time on 10 successive cases treated in this fashion, with crushing of the spur early, and closure of the ileostomy before serious nutritional disturbances can occur. Nine of the 10 cases recovered, a record which is indeed a milestone in a problem the literature of which has heretofore been devoted to failures.

At the University of Minnesota Hospitals, primary closed anastomosis was brought into use by one of these cases and pressed the more vigorously as experience was gained. The advantages of rapid restoration of gastrointestinal function, omission of a second operation, and shortened hospital stay seem to us to be arguments in favor of the method. It must be granted that good fortune has played a major role in more than one of these cases and that the mortality record can hardly remain perfect. It is with some misgivings that so small a series is presented.

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\* After submission of this paper for publication, the son of one of our surgery residents, age 3, #737852, was admitted for intussusception of 17 hours' duration, on May 23, 1947. It was reduced by barium enema, but recurred 27 hours later. Exploration showed an easily reducible intussusception at the ileocecal junction, which was patulous. Palpation through the inverted cecal wall revealed polypoid masses in the last 3 cm. of ileum. In the belief this situation underlay the recurrence of the intussusception, the terminal ileum was resected, the cecal stoma was closed, the appendix was removed, and a one-layer, silk, end-to-side anastomosis was made to the ascending colon. The postoperative course was uneventful and the patient is well today. The specimen showed a congested Peyer's patch with erosion on the surface.

## THE TYPE OF ANASTOMOSIS

In the earliest cases the Martzloff-Burget plan was employed. It is not satisfactory in very slender segments of intestine, however, and for this reason the oblique, aseptic anastomosis with rotation was later employed.<sup>3</sup> More recently, the single-layer silk method used in the last case was adopted.

*Method* Anastomosis clamps are placed somewhat obliquely and not quite completely across the prepared bowel about 1 cm from the remaining edge of mesentery (Fig 1). The bowel is cut across with cautery as with either of the older methods. Halsted silk (2½-pound test) sutures are placed 7 mm back from the cut edge of the intestine to be anastomosed (not from the clamp), they are placed first on the back side of the anastomosis and tied, closing the bowel over one blade of both anastomosis clamps. The clamps are then swung to the other side so the anterior wall of bowel can be similarly sutured and tied. Proper initial clamp placement permits closure over the tips of the clamps also. The entire suture line is now complete except at the point of exit of the clamps. Preplacement of two sutures here permits completion of the anastomosis at once after careful removal of the clamps.

In case of questionable viability, wide variation in diameter of the ends to be sutured, or somewhat narrow lumen, the clamps may be placed more obliquely and one end rotated, as in the oblique, end-to-end anastomosis previously described.<sup>3\*</sup>

That multiple-layer catgut anastomoses of stomach and intestine should have achieved and maintained general use is perplexing in the face of the demonstration by Halsted of the efficacy and safety of the single-layer silk

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\* In case of difficulty in closing the bowel over the two clamps in cases in which the diameter of one or both sides is small, loosening or removal of the clamp from the distal or empty segment alone permits easy closure except at the point of exit of the clamp or clamps, this may be facilitated by the use of Lembert instead of Halsted stitches.

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FIG 1—Closed, one-layer, interrupted silk anastomosis

a) Placement of first Halsted mattress sutures. Note that the clamps are placed not quite completely across the bowel. The point of exit of sutures closest to the modified Martzloff clamp is 7 mm from the cut edge of the bowel. If the bowel is less than 2 cm in diameter, either smaller clamps may be used, or the sutures may be placed immediately adjacent to the clamps and the clamps removed before tying the stitches,<sup>18</sup> or, preferably, the two-layer, oblique, end-to-end anastomosis may be used,<sup>3</sup> best with withdrawal of the inner catgut basting stitch after completion of the silk suture line. When the distance from the cut edge of the bowel to the stitches is more than one-third the length of tissue along the crushing clamps, real danger of obstruction is present.

b) Completion of back side of anastomosis, tying also over ends of clamps.

c) and d) Front side of anastomosis.

e) Removal of clamps—delayed until all but two sutures have been tied.

f) Completion of anastomosis by tying last two sutures after removal of clamps. The total number of sutures for intestinal anastomosis has varied from 11 to 18.

# GANGRENOUS INTUSSUSCEPTIONS

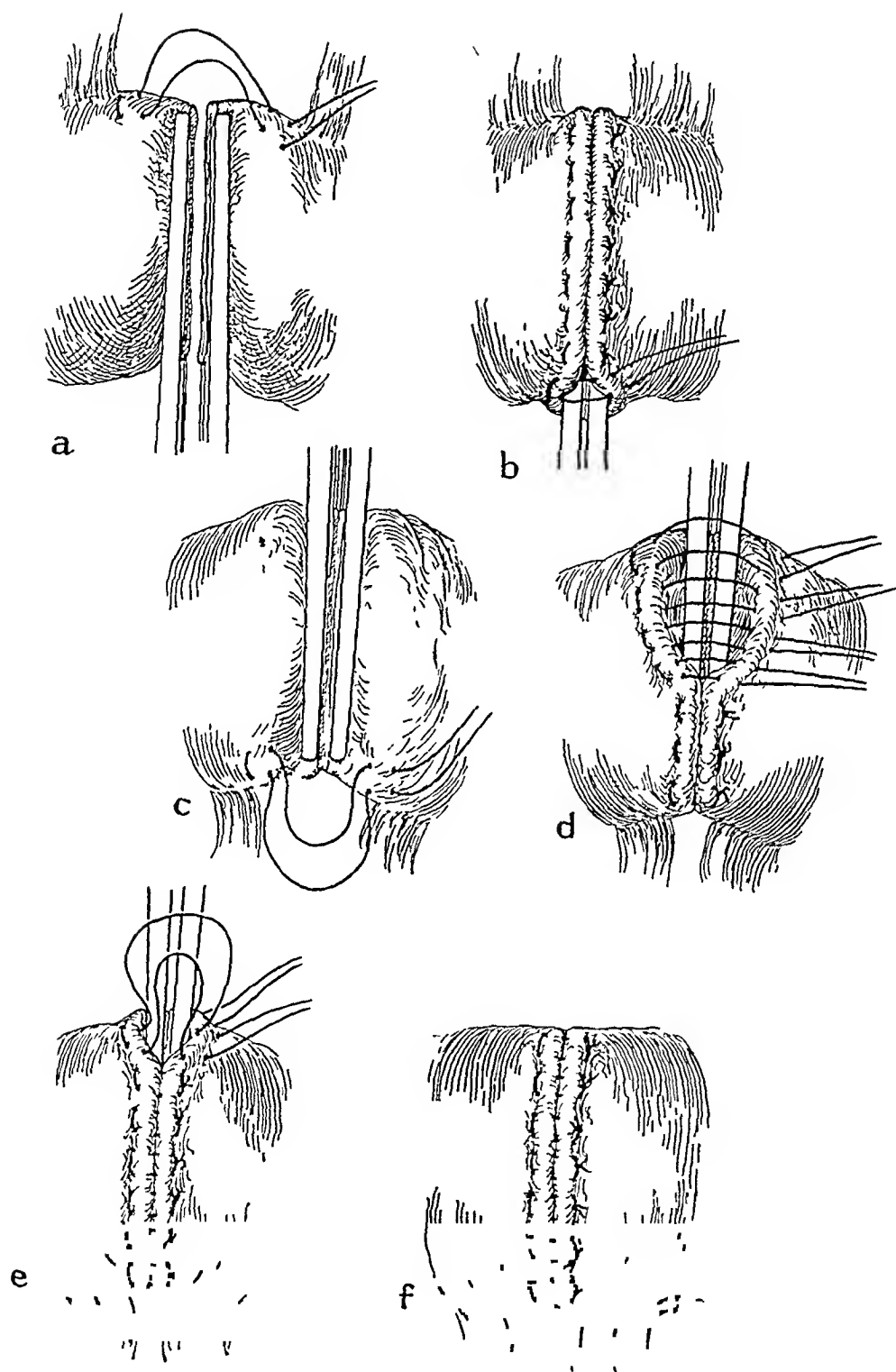


FIG 1



anastomosis in dogs. It is true that without the closed method introduced to general use by Collins, by Scarff, and by Martzloff and Burget, the silk technique was more cumbersome to use. The feasibility of single-layer silk anastomoses over clamps, as proposed by Scarff, was doubted by Martzloff and Burget because of fear of over-inversion of tissue. F. K. Collins presented a method of end-to-end anastomosis in which the clamp was used only to make secure a previously laid tie about the intestine. His method accomplishes nicely serosal approximation without contamination, but suffers seriously from overinversion of tissue, in the light of my own bad experience. The same criticism seems to hold against the bulkhead method, even as so ingeniously modified by Horne, except in the rectal region, where large diameter and ready proctoscopic availability insure against serious obstruction.

At the University of Minnesota Hospitals, reapplication of the bulkhead method has proven successful for low rectal anastomoses, and Wangensteen had previously found single-layer anastomoses over clamps very satisfactory in the gastroenterostomy of gastric resection, and also in some colon and small bowel anastomoses. Besides the danger of overinversion, an objection to the use of single-layer interrupted silk anastomoses over clamps lies in the possibility of soiling in the process of removing the clamps before the numerous sutures have been tied. It is primarily this that the present method attempts to avoid.

The safety of such an anastomosis was suggested by removal of an inner running catgut stitch because of pursestring effect in ileosigmoidostomy after colectomy for ulcerative colitis in September, 1946. This left a true single line of sutures, whereas Wangensteen's anastomosis is usually done with placement of 30 to 40 sutures, with some staggering so as to accomplish approximation in a broader area than a true single line.

The anastomosis as illustrated above has been used in 19 cases, 5 in the presence of small bowel distention from obstruction. All cases have recovered smoothly save one who had perforation of an obstructed closed loop with generalized peritonitis before surgery and one who had anastomosis of a sigmoid colon after removal of an area of diverticulitis. In the latter case the bowel was 15 mm in external diameter, and the sutures were placed 8 mm back from the clamps, with a transverse suture line. Although it was later found a catheter could be passed easily through the anastomosis, the inverted cuffs behaved in valve-like fashion sufficient to cause fatal tension gangrene of the transverse colon. In cases in which the sutures have been placed back of the cut edge of the bowel less than one-third the length of crushed tissue in the anastomosis clamp, there has been no complication.

This conclusion as to amount of inversion has been borne out by trial anastomoses in bowel obtained at autopsy. By use of a 7 mm distance from the cut edge of the bowel—not from the clamp—it is possible to achieve approximation over the modified Martzloff clamps devised for the oblique anastomosis.<sup>3</sup> Anastomoses so constructed allow free flow of water at less than 1 cm head of pressure. Intestine less than 2 cm in diameter

seems more safely anastomosed by the previously described two-layer oblique anastomosis with rotation, with withdrawal of the catgut basting stitch after placement of the silk if desired

Adoption of this type of procedure was entertained initially as a time-saving measure. It seems regularly, however, to have been followed by a shorter period of postoperative ileus than anastomoses with one layer of catgut in addition to silk (Note case 8, put successfully on feedings two days after operation). Proctoscopic examination of patients who have had bulkhead rectal anastomoses indicates the inverted tissue remains soft and pliable as opposed to the inverted cuffs containing catgut, which are rigid.<sup>3</sup> It is possible that the reaction to catgut found in experimental anastomoses, and not found to such an extent by Mall, by Sabin, and by Scarff in silk anastomoses, accounts for both the delayed mucosal healing and the more prolonged ileus in the catgut anastomoses. It seems inescapable that it contributes to the persistence of the inverted ridge at the suture line.

A final factor in favor of this procedure is that it possesses neatness and simplicity, and freedom from complicated or risky manipulations. It is best for the surgeon to familiarize himself with the method in the dog before applying it to human patients.

#### SUMMARY

1 Between November 1, 1940, and March 1, 1947, eight resections have been done in caring for intussusceptions at the University of Minnesota Hospitals. One had exteriorization and delayed closure, and seven had primary, aseptic anastomosis. All patients recovered.

2 The indications for resection were

Infarction of intussusceptum	5 cases
Recurrent intussusception with polypoid Peyer's patch	1 case
Developing recurrence while observing for viability, and Meckel's diverticulum	1 case
Irreducible intussusception due to a large polyp	1 case

3 The choice of procedure lies between exteriorization and early closure on the one hand, and resection and primary closed anastomosis on the other. With a background of closed anastomoses, the latter course is preferred here.

4 A simple, safe type of one-layer silk, closed anastomosis is presented.

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# MEDIASTINAL ABERRANT GOITER\*

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PARTIALLY INTRATHORACIC GOITERS are very common, especially in the endemic goiter areas (10 to 15% of all cases<sup>7, 13, 17, 19, 25, 33</sup>) and aberrant thyroid tissue not infrequently has been encountered in the neck, but aberrant intrathoracic goiters are very rare. A review of the medical literature in the English language for the past ten years reveals only 14 unquestionable cases, including six collected from the European literature by Mora, Isaacs, *et al*<sup>25</sup>

Crile,<sup>6</sup> Smith,<sup>28</sup> and Touroff<sup>30</sup> and others have reported multiple papillary carcinomatous masses in the thorax that may have developed from aberrant thyroid tissue but may well have been metastases rather than primary tumors, so they are not included in the table.

It is extremely probable that aberrant thyroid tissue is much more common than these reports indicate, for not one report of normal thyroid tissue in this area was found. All except the cases of carcinoma showed the pathology of nodular goiter, either toxic or non-toxic, and a majority were associated with nodular goiters in the neck. This parallels closely the pathology of partially substernal goiters which always result from the growth of large nodular glands in the neck.

It is noteworthy that several authors<sup>6, 19, 33</sup> report huge numbers of goiters without a single aberrant mass in the thorax and that more than one leading authority<sup>19, 31</sup> has expressed doubt as to the existence of this anomaly.

Blades,<sup>2</sup> in his report of 109 cases of mediastinal tumors in the Army of the United States, mentions only two of thyroid origin. These cases were not included in the table because of insufficient data. The fact that almost if not all of these tumors were in males is probably a factor in his series.

## CLASSIFICATION

The lack of a standard classification for intrathoracic tumors of thyroid origin makes it difficult to be sure of one's ground in a study of the literature, and some case reports may have been missed for this reason. I would like to suggest a classification that, while it is somewhat clumsy, is at least free from ambiguity. It is not original except in so far as sharpness of definition is involved.

## INTRATHORACIC GOITER

- I Aberrant Mediastinal Goiter
- II Substernal Goiter

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A Complete

B Partial

1 Intermittent

2 Constant

a First degree (less than one-half)

b Second degree (more than one-half)

TABLE I

Author	Location	Attachment	Blood Supply	Approach	No Cases
Mora <sup>23</sup> et al	Posterior superior mediastinum	Not definitely stated, probably to left lobe of thyroid	From neck, origin not definitely stated	Cervical	1
The Berards <sup>1</sup>	Retro-esophageal	Not stated	Not stated	Cervical	1
Von Haberer <sup>22</sup>	Multiple masses in chain to posterior mediastinum	Left lobe of thyroid	Not stated	Trans sternal	1
Roholm <sup>28</sup>	Retro esophageal	Unknown	Unknown	No operation aspiration biopsy	1
Urban <sup>31</sup>	Retro mediastinal	Not stated	Not stated	Cervical	2
Henschen <sup>19</sup>	Retro esophageal	Thin process to cervical goiter	Not stated	Not stated	1
Hicken <sup>13</sup>	' Deeper portion of chest cavity	None to thyroid gland	Not stated, not from neck	Discovered at autopsy	1
Hollenberg <sup>14</sup>	Anterior mediastinum	Fibrous band to neck	From neck, probably inferior thyroid	Cervical	1
Eggers <sup>9</sup>	Anterior mediastinum	None to neck	Not stated	Trans-sternal	1
deCourcy <sup>7</sup> and Price	Anterior mediastinum	Fibrous band to trachea in neck	Not identified, not from neck	Trans sternal	1
Mason <sup>21</sup>	Right posterior mediastinum	No cervical attachment	Not identified	Posterior extra-pleural mediastinotomy	1
Cabot case <sup>3</sup> 22352	Right mediastinum on diaphragm	Vascular pedicle upward	From above, source not identified	Posterolateral transpleural mediastinotomy	1
Soley <sup>29</sup>	Right mediastinum touching diaphragm	Vascular pedicle to neck	From neck, source not identified	Autopsy	1
Author	Anterior superior mediastinum	None in neck	From mediastinum, probably thyroid ima	Cervical	1
Author	Anterior superior mediastinum	None in neck	From mediastinal vessels, aorta probable source	Anterior trans-pleural mediastinotomy	1
Author	Retro esophageal	Vascular pedicle posterior to subclavian	From above, probably from subclavian artery	Posterior transpleural mediastinotomy	1

I *Aberrant Mediastinal goiter* should include all thyroid tumors that lie entirely below a plane extending from the superior surface of the first thoracic vertebra to the suprasternal notch, that are either entirely unconnected with

the thyroid gland proper or are at most connected by a fibrous band. If connected by such a band, they should lie in such a position that the mechanism of Lahey<sup>19</sup> can not conceivably have displaced them to that position from the neck (for example, the case of Churchill<sup>3</sup> that rested on the right leaf of the diaphragm)

The contention that any mass connected with the thyroid gland in any way must necessarily have been forced downward from the neck is unsound. It is reasonable to suppose that masses that descend into the chest during fetal life may retain a connection to the parent gland. However, it must be admitted that if a definite attachment is found and the tumor lies in such a position that it might have been forced down from the neck, there is serious doubt as to its origin. Such cases must be considered questionable. It does not seem reasonable to assume that a mediastinal goiter resting on the diaphragm was displaced from the cervical region to its final position by mechanical means simply because its vascular pedicle extended upward. A mass of aberrant tissue may continue to descend after its vascular connections have been established, just as the thyroid gland itself does after picking up the superior thyroid artery.

II A *Substernal goiter, complete*, should include only those uncommon cases in which the entire thyroid gland lies within the thorax. The term is frequently used to include thyroids that lie almost entirely in the mediastinum and on this basis it is reported that about 1% of all nodular goiters are in this class. It is probable that completely intra-thoracic glands are actually quite rare.

II B 1 *Substernal goiter, partial intermittent*, should include the "plunging goiters" that slip into and out of the chest cavity during the act of swallowing or during changes in position of the neck.

II B 2 *Substernal goiter, partial constant*, first and second degree, require no explanation. Many of those spoken of as completely substernal probably belong in this group.

Since the term "substernal goiter" is in common use for glands partially displaced into the mediastinum and since practically all such tumors lie in a substernal position, it seems logical to reserve this term for such cases. On the other hand, since aberrant thyroid tissue may lie anywhere in the mediastinum, the broader term mediastinal seems more appropriate.

#### CLINICAL SIGNIFICANCE

A sharp separation of aberrant tumors from those mechanically displaced into the chest is important not only on purely scientific grounds but also for clinical reasons. Substernal goiters, having been displaced from the neck into the mediastinum by the mechanism so graphically described by Lahey,<sup>19</sup> almost, if not always, lie in the anterior compartment of the superior mediastinum in front of the trachea, the great vessels and the recurrent nerves, and are directly connected to or continuous with the thyroid gland proper. They almost if not always derive their blood supply from the inferior thyroid

vessels Therefore, if those vessels are secured, the substernal mass or masses can safely be displaced into the neck by traction, blunt dissection, coughing (by the patient), or by any combination of these three, after which they can be removed without great difficulty, and without undue danger of hemorrhage or of injury to the recurrent nerves If such a mass is too large to permit its delivery intact, it can be eviscerated by Lahey's method, after which it can be delivered and removed as a smaller mass would be

The safety of the above mentioned procedures depends upon the anatomic relations previously described, and especially upon the fact that the blood supply of the tumor is accessible from the neck In view of the fact that the thyroid anlage originates at what will become the base of the tongue and descends anterior to the larynx and trachea, it seems highly probable that most aberrant thyroid tissue will be found in the same location and with the same blood supply as the substernal portion of a substernal goiter Under these circumstances, the mass can and should be removed by the same methods In fact, it seems probable that many aberrant thyroid masses have been so removed without special comment by the operator

If, however, the mass does not lie in the classical location, if it does not have the usual relation to the great vessels, the trachea, the esophagus, and the recurrent nerves, if it does not receive its blood supply from vessels accessible from the neck, any attempt to remove it by the usual technic may be unsuccessful or disastrous

I have had what appears to be the unusual experience of encountering three aberrant mediastinal goiters that illustrated most of the problems that may arise

#### CASE HISTORIES

**Case 1**—Mrs M K, white female, age 50 years, was admitted to Touro Infirmary April 5, 1939 She complained of a large cervical goiter of two years' duration and of dysphagia that has become progressively worse for one year There was no dyspnea There were no signs nor symptoms of thyrotoxicosis

Physical examination showed nothing of note except a large nodular goiter, the isthmus of which extended below the supra-sternal notch Both vocal cords moved freely

X-ray examination showed "a wedge-shaped widening of the superior mediastinal shadow, which is associated with a dextro displacement of the trachea suggesting a substernal extension of an enlarged thyroid" Unfortunately, these x-ray films have been lost

Routine laboratory examinations showed nothing of significance

Operation, April 28, 1939 Under ethylene anesthesia (not intratracheal) the usual collar incision was made, the infra hyoid muscles divided, and a subtotal resection of the right lobe and a total removal of the isthmus and left lobe of the thyroid were carried out. Two substernal masses entirely separate from the cervical goiter were found One lay behind the right sterno-clavicular joint and a larger one was directly behind the sternum Both were freely movable and were delivered into the neck by gentle traction There was no bleeding The mass on the right had a long vascular pedicle that extended into the mediastinum The centrally located mass had no organized vascular pedicle Neither received its blood supply from the inferior thyroid vessels

The operative field was dry and exposure was excellent at all times, in spite of which bilateral vocal cord paralysis occurred Dyspnea became progressively worse and on the

following morning tracheotomy became necessary. Fortunately, no wound infection resulted, and she was discharged on the 15th postoperative day, in excellent condition except for the vocal cord paralysis.

*Pathologic report*—The two substernal masses measured 6 x 5 x 3 cm and 4 x 2 x 2 cm respectively.

*Diagnosis*—Nodular nontoxic goiter with cystic change and some calcification\*.

*Comment*—In this instance there were two separate masses in the anterior compartment of the superior mediastinum, entirely unconnected with the thyroid gland proper, and deriving their blood supply from some mediastinal vessel or vessels, perhaps a thyroid ima. Both tumors were easily displaced into the neck and removed in a dry field with the blood supply under visual control, so no danger of hemorrhage existed, but in spite of this satisfactory exposure both recurrent nerves were permanently damaged or severed. Since they were not dissected out, I cannot be sure how or where they were injured, but in view of the excellent exposure and the very dry field at all stages of the operation, I am quite certain that the nerves were not cut or ligated at any point in their usual courses. It is an interesting fact that the first signs of respiratory distress occurred 15 minutes after the resection had been completed. I suspect that these tumors lay between the nerves, and that they were stretched or torn during the delivery of the masses into the neck. Probably one cannot fully depend upon the often-repeated statement that the recurrent nerves always lie behind substernal goiters, and should in such cases expose them as Lahey has urged in all thyroidectomies.

**Case 2**—E. W., colored female, age 45, was admitted to Charity Hospital on April 3, 1945, complaining of shortness of breath when lying down and on exertion. Nausea frequently followed the dyspnea. She also complained of sweating, nervousness, palpitation, and swelling of the ankles.

In September, 1940, she had had a subtotal thyroidectomy performed by me for a huge calcified nontoxic nodular goiter. A similar mass was recognized in the chest, and diagnosed substernal goiter (Fig 1), but at operation no connection with the thyroid gland nor its blood supply could be found. No attempt was made to remove it from above because of its huge size and the uncertainty as to its blood supply. The patient declined further surgery and was not seen again by us until the above date. She was, however, observed intermittently in the medical clinic.

On this admission examination showed blood pressure 170/100, pulse 120, respiration 28. The chest showed physical signs of a large mass in the anterior superior mediastinum and of fluid in the left pleural cavity. The heart was markedly enlarged and a soft systolic murmur was heard at the apex. The liver was enlarged and tender and the spleen was palpable. X-ray examination showed the large partially calcified substernal mass practically unchanged since the first operation.

The E. K. G. showed definite evidence of myocardial disease.

The medical department made a diagnosis of congestive heart failure complicated by a large mediastinal tumor, probably of thyroid origin. Engorgement of the neck veins and increased venous pressure were considered to be due to cardiac failure rather than to the tumor. Under bed rest and medical treatment the cardiac condition improved markedly, but finally a point was reached at which it was believed no further improvement could be expected without removal of the tumor which pressed upon the heart and great vessels.

X-ray examination at this time showed a huge mass in the anterior compartment of the mediastinum (Figs 2 and 3). It extended from the supra-sternal notch to the 5th rib anteriorly and occupied one half the transverse diameter of the chest cavity, being slightly more prominent on the left side. The trachea was displaced moderately to the right.

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\* At a later date Brien King's operation was performed and the laryngeal obstruction relieved.



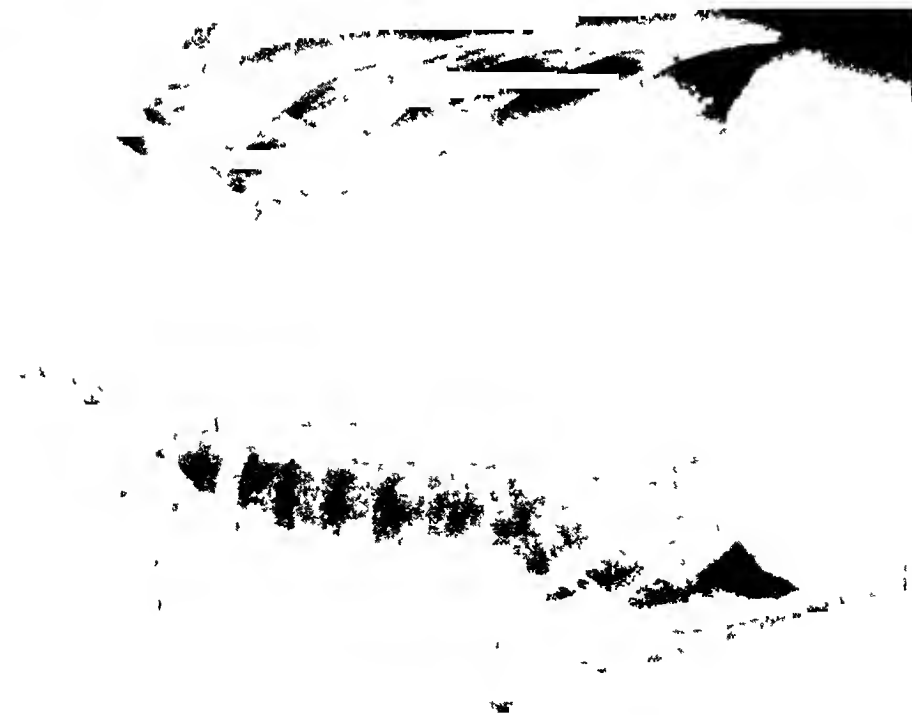


FIG 1—Case 2 Roentgenogram showing huge calcified cervical goiter and similar mass in mediastinum



FIG 2 — Case 2 Roentgenograms after cervical thyroidectomy, showing large calcified mass in anterior-superior mediastinum with displacement of trachea to the right

Operation, April 25, 1945 Anesthesia Intratracheal ethylene-ether An anterior approach was made through the 2nd interspace with division of the 2nd and 3rd costal cartilages The tumor bulged far into the left hemithorax and was covered only by the pleura, which was freely incised anterior to the phrenic nerve By combined blunt and sharp dissection, the mass was freed from its bed and delivered into the left chest cavity



FIG 3 — Case 2 Roentgenograms after cervical thyroidectomy, showing large calcified mass in anterior-superior mediastinum with displacement of trachea to the right

This dissection was tedious because of numerous strong fibrous attachments but was not unduly difficult because of the excellent exposure In order to expose the right side of the tumor the sternum was divided transversely shortly before the completion of the dissection One large artery entered the mass on its posterior aspect about 3 or 4 cm below the concavity of the arch of the aorta

A large mediastinal cavity remained, so the mediastinal pleura, now redundant, was attached to the anterior chest wall so that the costal pleura could be completely closed,

while leaving a small opening into the mediastinal cavity, which was loosely packed with dry gauze. The pleural cavity was closed without drainage. The mediastinal pack was removed in 48 hours but a slight hemorrhage occurred on the following day, so it was replaced for 48 hours more. Moderate drainage but no active infection persisted for ten days, after which her convalescence was uneventful. The cardiac status improved considerably, but not completely, and her activities are still somewhat restricted, but failure has not recurred (Fig 4).

*Pathologic report*—A nodular tumor weighing 426 Gm and measuring 15 x 10 x 5 cm

*Diagnosis*—Fetal adenoma with fibrosis, calcification, hemorrhage, and cyst formation



FIG 4—Case 2 Roentgenogram after removal of intrathoracic goiter

*Comment*—In this case there was a single very large mass in the anterior compartment of the mediastinum extending well below the arch of the aorta. Its location and anatomic relations were exactly those of a large substernal goiter, but it was entirely unconnected with the thyroid gland proper and did not receive its blood supply from a cervical vessel. It was supplied by a single large artery that entered its left posterior aspect well below the aortic arch, from which it probably arose.

Any attempt to remove this mass through a cervical incision would, in my opinion, have been either unsuccessful or fatal, or both. On the other hand, the anterior transpleural approach employed provided free exposure at all times, all points of attachment being divided under direct vision.

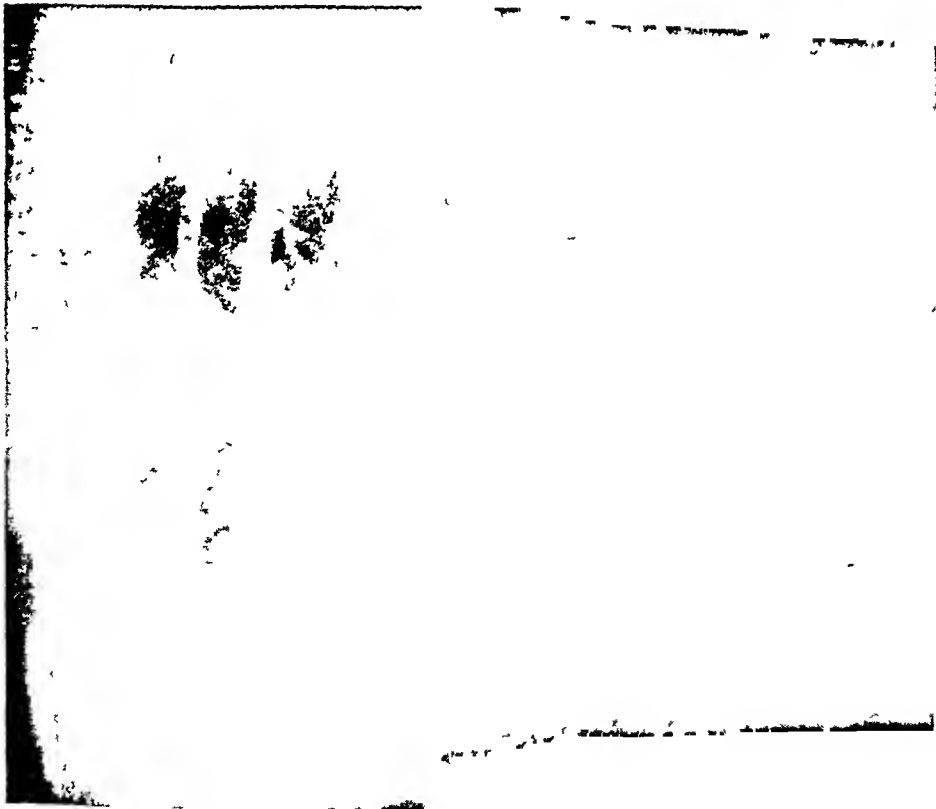


Fig 5—Case 3 Roentgenogram showing mediastinal mass projecting into the right lung field remaining after thyroidectomy



Fig 6—Case 3 Roentgenograms with visualization of esophagus, showing the increased size of the mediastinal mass and the fact that it causes displacement of the esophagus anteriorly and to the left

**Case 3**—Mrs M C, white female, age 42 years, was admitted to Touro Infirmary on June 25, 1944, complaining of a tumor in the chest

In May, 1933, a subtotal thyroidectomy had been performed for a mildly toxic nodular goiter. A diagnosis of intrathoracic goiter was made at that time, but at operation the intrathoracic mass could not be located from the cervical incision (Fig 5)

She had been in excellent health since this operation, and the intrathoracic mass produced no symptoms, but repeated x-ray observation showed that it was steadily



FIG 7—Case 3. Roentgenograms with visualization of esophagus, showing the increased size of the mediastinal mass and the fact that it causes displacement of the esophagus anteriorly and to the left

increasing in size. The last roentgenogram revealed a large, roughly spherical mass posterior and to the right of the esophagus and projecting well into the right lung field (Figs 6 and 7) opposite the 1st to the 6th thoracic vertebral bodies.

Physical examination showed nothing of note. Both vocal cords moved freely. The electrocardiogram was negative. Hematology showed a mild secondary anemia.

Operation, June 27, 1944. Anesthesia: Intratracheal cyclopropane. A posterior transpleural approach, with resection of the 4th and division of the 3rd and 5th ribs, was made. Exposure was excellent. The tumor was seen to project well into the apex of the right pleural cavity and to lie directly upon the bodies of the vertebrae. It was covered laterally only by the pleura, which was incised posterior to the phrenic nerve. The tumor was easily shelled out and had only one firm attachment, its vascular pedicle, which descended

behind the subclavian artery to the upper pole of the mass. This pedicle was ligated and divided. The rent in the mediastinal pleura was sutured and the chest cavity closed without drainage.

The postoperative course was uneventful and she was discharged on the 12th postoperative day.

*Pathologic report*—"A tumor weighing 212 Gm. roughly ovoid in shape approximately 12 x 9 cm."

*Diagnosis*—"Adenoma of aberrant thyroid tissue" (Fig 8)

*Comment*—This case shows a complete deviation from the normal in the descent of thyroid tissue into the thorax. The tumor lay in the posterior compartment of the

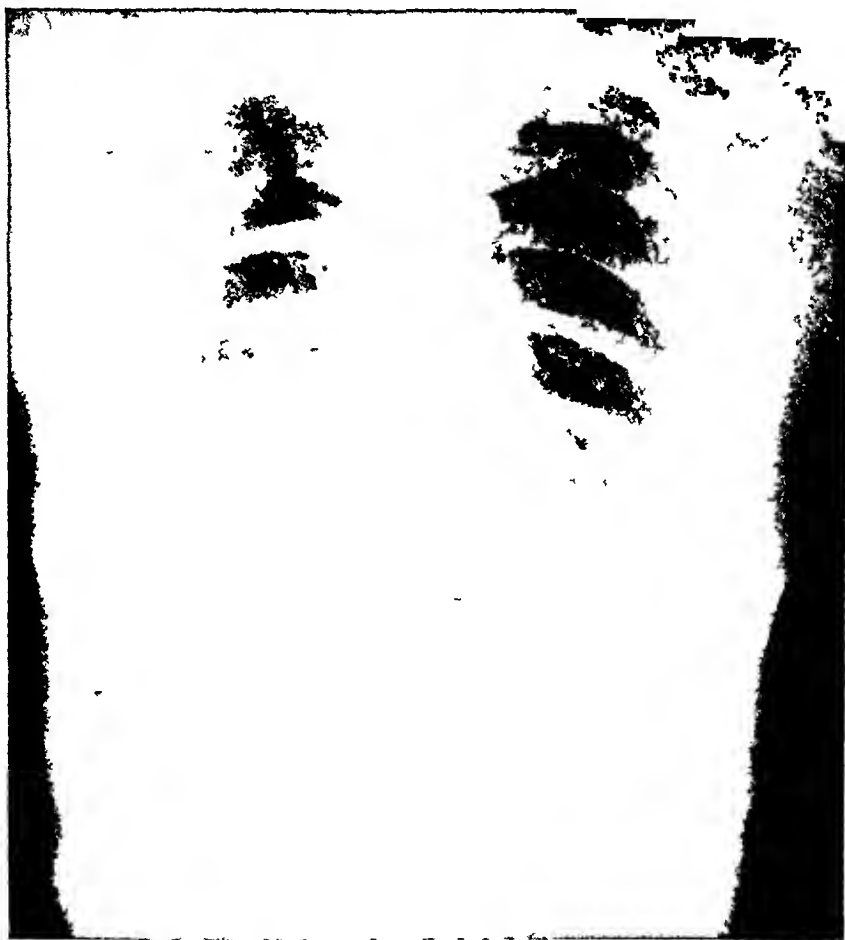


FIG 8—Case 3. Roentgenogram after removal of mediastinal aberrant goiter.

mediastinum, behind and to the right of both trachea and esophagus. It probably derived its blood supply from a branch of the subclavian artery, but this artery descended behind the subclavian trunk. Mediastinal thyroid masses have been removed from similar locations through cervical incisions, when a band of fascia connected them to the cervical gland, but if the blood supply cannot be secured before delivering the mass, it is a very dangerous procedure. In this instance the vessels would almost certainly have been avulsed and would then have retreated behind the subclavian artery, a most disconcerting situation.

#### OPERATIVE PROCEDURES

*Anesthesia* I believe that general inhalation anesthesia, administered through a semi-rigid intratracheal tube, is preferable for all substernal or

mediastinal goiters Several authors of wide experience have recommended local anesthesia chiefly because the patient can cough and help in the delivery of the substernal mass, but a skilled anesthetist can lighten the anesthesia and get the same effect at will, and the assurance of a clear airway at all times during manipulation about a displaced and distorted trachea is of paramount importance It is also highly desirable to be able to inflate the lung or lungs if the pleural cavity should be opened

*Approach* Mediastinal goiters, aberrant or otherwise, that lie in the anterior compartment of the mediastinum and derive their blood supply from vessels that are accessible from the neck should undoubtedly be removed by the cervical approach even if they should be so large that evisceration is necessary before delivery can be effected If, however, the blood supply cannot be identified and controlled from above, any attempt to remove the mass by this route may be disastrous

Splitting the sternum to expose large substernal tumors has been tried by many surgeons, but both failures and fatalities have been numerous<sup>6, 7, 8</sup> This approach gives a poor exposure since the opening is limited by the shortness and rigidity of the first ribs, and the bony margins of the opening are completely inflexible The substernal space is very vascular and hemorrhage, usually venous, may be severe and hard to control The pleural cavities approach each other closely in the midline and often overlap, so one or both are frequently opened Small inaccessible tears in the pleura are likely to result in tension pneumothorax, because air is sucked in with each inspiration, whereas in expiration the pleura bulges against the chest wall and closes the opening, thus trapping the air in the pleural cavity Any attempt by the anesthetist to inflate the lung fails for the same reason I have observed one operative death caused by this mechanism (not in a mediastinotomy), which incidentally can be easily corrected by opening the pleural cavity widely, and thus permitting escape of the trapped air It is for these reasons among others that I prefer a transpleural approach to any mediastinal goiter that cannot be removed solely by the cervical route

Almost all mediastinal tumors tend to expand into one or the other lung field since that is the direction of least resistance The approach may be made from that side, anteriorly or posteriorly as the location of the mass dictates The size and location of the tumor will determine whether or not rib resection is required In general very large tumors and high posterior approaches require rib resection, whereas small tumors and low or anterior approaches do not

When a wide transpleural opening is made, more than half of the tumor is usually clearly visible, together with the heart and great vessels and the phrenic and vagus nerves With this free exposure the dissection can be planned with almost all important structures in full view As compared with the extra pleural approach, the dissection required is almost 50 per cent less and the visibility almost infinitely better

CONCLUSIONS

1 The classifications of intrathoracic goiters in common use are variable and confusing A method of classification is proposed

2 Aberrant mediastinal goiters are rare Fourteen cases have been collected from the English medical literature of the past ten years This number includes six cases from the European literature collected by Mora et al<sup>25</sup> Three cases are added

3 The cervical approach is preferable for all intrathoracic goiters located in the anterior compartment of the mediastinum and receiving their blood supply from vessels accessible from the neck, but a transpleural approach is desirable for all others

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State of Pennsylvania } ss  
County of Philadelphia }

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Before me, a Notary Public in and for the State and county aforesaid, personally appeared J R Arnold, who having been duly sworn according to law deposes and says that he is the Treasurer of the ANNALS OF SURGERY and that the following is, to the best of his knowledge and belief, a true statement of the ownership, management (and if a daily paper, the circulation), etc, of the aforesaid publication for the date shown in the above caption, required by the Act of August 24, 1912, as amended by the Act of March 3, 1933, embodied in section 537, Postal Laws and Regulations, printed on the reverse of this form to wit:

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[Signed] J R ARNOLD

Affirmed to and subscribed before me this 19th day of September, 1947

[Seal]

HARRY J BEARD

(My commission expires March 5, 1949)

## INFLAMMATORY OBLITERATION OF THE COMMON AND HEPATIC DUCTS FOLLOWING CHOLECYSTECTOMY\*

HENRY F GRAHAM, M D

BROOKLYN, N Y

A B, A WOMAN 41 YEARS OLD, has had 5 children When first seen on February 18, 1942, she gave a history of attacks of severe epigastric pain that had commenced four years ago, one month after parturition Recently the acute attacks had ceased but had been replaced by a burning sensation in the right upper quadrant of the abdomen There was no history of jaundice or clay-colored stools

Examination showed tenderness over the gall bladder and appendix An X-ray showed stones in the gallbladder On March 25, 1942, a cholecystectomy and appendectomy were performed under ether anesthesia at the Methodist Hospital A soft rubber tube drain was inserted beneath the liver The gallbladder was large and full of numerous stones The operation was an easy one and took one hour and 15 minutes The pathologic report showed atrophy of the mucosa of the gallbladder, slight thickening of the wall and infiltration with a few round cells The diagnosis was chronic cholecystitis and cholelithiasis

Following operation there was occasional vomiting for 36 hours The dressing was stained with a little biliary discharge Two days after operation the sclerae were clear but the skin was a little muddy On the third day there was slight jaundice present On the fourth day she had two yellow and brown fluid evacuations There was a little pleurisy in the left lower chest On the fifth day tan colored formed feces were obtained There was still a little biliary discharge on the dressing On the sixth day the icteric index was 30 and the leucocytes were 10,900 with 80 per cent polynuclears A small amount of light yellow feces was evacuated at 2 P M but at 9 40 P M the first clay-colored stool was obtained, *i e*, six and a half days after operation From this time on the jaundice and clay-colored stools persisted

At the request of the husband, Dr Thomas M Brennan, an attending surgeon to two large Brooklyn hospitals, then saw her in consultation It was evident that an obstructive jaundice was present and a second operation was performed on April 5, 1946, the 11th day after the original operation Doctor Brennan was present at the operating table as an observer and Dr Pierre A Renaud, an attending surgeon to the Methodist Hospital, was first assistant An incision was made through the old scar beneath the ribs on the right side and extending one inch further laterally Adhesions were separated with difficulty, exposing the region of the common duct and Foramen of Winslow No accumulation of bile was found The entire edge of the Gastrohepatic

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\* Read before the Meeting of the American Surgical Association, March 25-27, 1947 Hot Springs, Va

omentum was thickened to about an inch in diameter from the fissure in the liver to the duodenum. After careful dissection and aspiration with a needle and syringe it was impossible to locate the position of the common duct. Attempts with a thumb forceps finally secured a free flow of bile, probably from the left hepatic duct as a probe could be passed upward and to the left but could not be passed downward into the common duct or upward to the right. As the operation had been prolonged and the condition of the patient was uncertain a small catheter was passed into the duct and fastened and the abdominal wall closed around a larger tube. The time of this operation was one hour and 45 minutes. No evidence was found that the common duct had been clamped, tied or cut or injured in any way at the first operation. Doctors Brennan and Renaud concurred in this opinion.

Following this second operation the jaundice finally cleared up, although the stools remained acholic. The patient was discharged from the hospital on May 2, 1942, with a tube and persistent biliary fistula. From July 1942 to April 1943 three further operations were performed by a surgeon in another city. The last one was a suture of the distal end of the common duct (exposed behind the duodenum) to a biliary duct in the fissure of the liver over a T tube. There was no evidence of any proximal portion of the common duct or of either hepatic duct.

Still later another operation was performed by a different surgeon who drew the duodenum up and performed an anastomosis in the fissure of the liver with some improvement on latest report. Such an experience as this is a tragic one for both patient and surgeon.

Although there are many references in the literature to "inflammatory stricture" most of them are brief and the condition is not well understood by internists or surgeons who are still prone to believe that all jaundice that follows operation and persists is due to an error in technic. Miller<sup>1</sup> states the situation well as follows, "Although the so-called diffuse stricture due to fibrosis of the wall of the common duct is not common, nevertheless, sufficient evidence is now at hand to warrant its recognition as well as indicate that it is a condition quite apart from congenital or traumatic stricture and probably quite different in mode of production from the strictures caused by gallstones. There seems good reason to consider it an inflammatory lesion which results in an essential fibrosis of the wall of the common duct. Neither traumatism or gallstones appear to be a factor in its causation."

Judd<sup>2</sup> believed that "Obliterative cholangitis resulting in stenosis of the common or hepatic duct is the cause of a considerable proportion of strictures of the common duct that have been classified as traumatic." He found that "in 16 out of 64 operations for stricture the condition was the result of obliterative cholangitis and in 15 more it might have been." Carter<sup>3</sup> discusses the "benign" type of cicatricial stenosis at length citing illustrative cases.

Dr John A. Timm, in a personal communication, reports a 30-year-old Puerto Rican who had no previous operation. He was markedly jaundiced. At operation Doctor Timm found sclerosis of the common, part of the cystic

and hepatic ducts with inflammatory induration of the omentum containing the portal structures. The pathologic conditions present were the same as in our case at the second operation. Walters<sup>4</sup> speaks of inflammatory stricture of the common ducts. He mentions one case in which there was a 15-year interval between cholecystectomy and the onset of obstructive symptoms. In his article for Lewis's *Practice of Surgery*<sup>5</sup> he says, "Occasionally the obliteration of the duct is due to an inflammatory process which destroys the mucosa lining the duct and converts it into a fibrous cord." Whipple<sup>6</sup> in Nelson's *Loose Leaf Surgery* speaks of "Stenosis of the ducts following trauma or inflammation." Lahey<sup>7</sup> also has seen "One case of complete obliteration of the bile duct undoubtedly due to an inflammatory process which completely destroyed the mucosa within the common and hepatic ducts converting that structure into a fibrous cord without a lumen." He says that for practical purposes nearly all the strictures of the common and hepatic ducts are man-made and reports a series of nine such strictures. It is interesting to note that he mentions the fact that the end of the duct proximal to the stricture was dilated in seven of the nine cases and, in the other two cases, he does not mention whether it was dilated or not. As most of the inflammatory strictures, like our case, show no dilatation above and an actual obliteration, even into the liver fissure, this seems an important differential point.

#### SUMMARY

Following an easy cholecystectomy there was evidence of obstructive jaundice. A second operation revealed an extensive cellulitis of the gastrohepatic omentum but no evidence of injury at the first operation. The cellulitis eventually terminated in a complete obliteration of some inches of the common and hepatic ducts. The absence of dilatation of the proximal portion of the duct is mentioned as a point in differential diagnosis.

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## THE APPENDICEAL STUMP\*

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IN THE TREATMENT OF ACUTE APPENDICITIS, there is apparently complete agreement that early operation is the only safe therapy. However, in relationship to the appendiceal stump, considerable variance of opinion exists regarding the proper operative technic.

Although the first appendectomy was performed as early as 1884, no general agreement exists regarding the preferable technic for management of the appendiceal stump. Authors in general do not seem satisfied with any specified method, but advocate their own particular technic because of end results. William Mayo, in explaining his preference for the technic he employed, summarized by saying, "I have not had occasion to regret not having inverted the stump."

Surgeons from various parts of the world, in statistically reporting large series of cases, apparently obtain comparable results. The majority reveal a tendency to advocate their particular method of management of the appendiceal stump, and also demonstrate a willingness to rationalize successful results obtained, as being due to the particular technic employed.

With such close correlation of statistical results and divergence of opinion regarding the manner of obtaining them, various methods of treating the appendiceal stump have been studied in an effort to determine whether or not the argument is academic or factual in character.

A series of rabbits were used for the study. The major interest was directed toward end results rather than interval. All animals were autopsied postoperatively. Gross and micro-pathology studies were made at 48 and 96 hour intervals as well as one week and one month. For purposes of clarity, discussion will be limited primarily to the observations noted at an interval of one month.

The three basic methods generally accepted for treating the appendiceal stump were employed, *e g*, (1) simple ligation (the "tie and drop" method), (2) ligation and inversion, (3) inversion without ligation. Each method was subjected to variable technics, with catgut, silk, phenol and cautery. Such variables are unimportant to this discussion, since they simply represent technical variations of accomplishing and demonstrating the underlying principles involved.

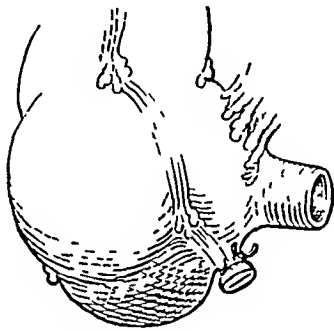
The method originally described by Dawbarn in 1895, of invagination of the appendiceal stump into the lumen of the cecum was not employed. In this article when reference is made to invagination of the stump, the term means into the wall of the cecum and not into the lumen. Common usage

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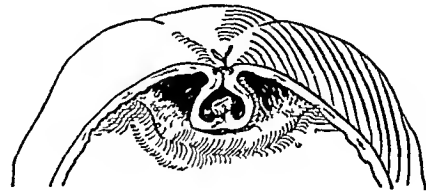
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has given a misconception to the terms—"invagination into the cecum"—and—"into the lumen of the cecum" What is accomplished in the usual technic of invagination, is the introduction of a blind pouch into the wall of the cecum and not into the lumen This applies whether the stump is, or is not, ligated Employment of the technic of anatomically true invagination of the stump into the lumen of the cecum involves technical difficulties that immeasurably increase the possibilities of fecal contamination

The conventional technics now employed are considered simpler and acceptable, and the end clinical results justify their use The original Dawbarn technic is a more formidable procedure than the standard methods, although in practice, it is more physiologic



*a "Tie and Drop"*



*b Inversion and  
ligature*



*c Inversion without  
ligature*



*d True invagination into the  
lumen of the caecum Original  
Dawbarn Technique This method  
was not used in this study*

FIG 1—Schematic representation of various methods of treating the appendiceal stump

Bickham, in describing operative technics, states that the canal of the appendiceal stump is probed to prove its patulousness and that it may be dilated with special forceps to aid invagination Such technic increases the hazards of fecal contamination

As pointed out by Dawbarn, to invert the stump into the cecal lumen and for it to drain therein, the stump of the appendix has to be turned completely outside in, or inside out Physiologic advantages of this procedure are nullified by the increased hazards of contamination and leakage

Deaver indicated that the important objects in appendectomy were (1) ligation of the base of the appendix, (2) removal without contamination, (3)

hemostasis. He further stated that if it could be accomplished satisfactorily, the stump of the appendix should be inverted.

Ochsner and Lilly, in 1937, reviewed the problem and indicated that inversion of the unligated stump was the method of choice. Their diagrams are illustrative of inversion into the cecal wall, although their terminology with non-ligation suggests an end result similar to the Dawbarn technic. Neither the technic advocated by Ochsner and Lilly, which is simply a slight modification of the Halstead "three clamp" method, nor by Goode and Kregel were employed in this study. Both methods basically, are variations of

invagination of the unligated stump into the wall of the cecum. The method of Goode and Kregel has the advantage of invaginating a small amount of stump into the cecal wall thereby minimizing tissue reaction in a closed sac.

Employment of a Cushing right angle stitch, Lembert stitch, or purse-string suture does not alter the final domicile of the appendiceal stump. If a residue of tissue is grasped by a clamp, pushed down and buried by any suture method, it "sits up" and does not "point down."

Adult rabbits, in preference to dogs, were selected for this study because of greater similarity to human intestinal anatomic characteristics. There were 44 experiments—25 with the buried stump and 19 with simple ligation.

At varying intervals (two days, four days, one week, and one month)

the animals were anesthetized and the appendiceal stump examined *in situ* and then removed for microscopic study.

Typical protocols, demonstrative of the three methods are presented. Evidence of inflammation, peritoneal contamination, cecal induration, necrosis and extent of adhesions were studied for comparative purposes. While many of the specimens revealed either one or a combination of these factors, no one method revealed dominant characteristics. It will be noted that the interval specimens in the inverted stump technics, on microscopic examination, revealed a greater degree of inflammatory reaction. Comparative end specimens, however, for all methods, microscopically and macroscopically, revealed little variation.

**Rabbit 1** "Tie and drop" (examined at 48 hours). Cecal area completely walled off by small intestine and mesentery. No evidence of peritonitis, no gross hemorrhage.



FIG 2—(Rabbit 3)—Section treated by simple ligation or "Tie and Drop," taken 32 days after operation.

*Laboratory Gross*—Stump not invaginated Serosa smooth except portion distal to ligature Ligature firm and intact *Microscopic*—Section showed marked inflammatory response about serosal and submucosal layers Several large areas of necrosis with slight hemorrhage into the tissue

Rabbit 2. "Tie and drop" (examined at 7 days) *Laboratory Gross*—Stump free and smooth Cecal area free of adhesions Serosa clean *Microscopic*—Slight fibrosis, no inflammation No necrosis, no hemorrhage

Rabbit 3 "Tie and drop" (examined at 32 days) Cecal area free of adhesions Encapsulated area in cecum resembled calcified node *Laboratory Gross*—Appendiceal stump completely covered by dense fibrous tissue On section, stump is firm and fibrosed *Microscopic*—Moderate fibrosis at margin of stump Low grade inflammation along margins of stump at site of organization Necrosis in central portion of stump No hemorrhage Reaction in tissues localized, slight

Rabbit 4 Ligation and Inversion (examined at 48 hours) *Laboratory Gross*—No adhesions about inverted stump Serosa clean Stump feels like hard fibrous nodule No infection or hemorrhage seen *Microscopic*—Marked inflammatory reaction with P M N cells Fibrosis over serosa No necrosis or hemorrhage Localized reaction in tissue

Rabbit 5 Ligation and Inversion (examined at 7 days) *Laboratory Gross*—Inverted stump covered by fibrous tissue with loops of bowel adherent *Microscopic*—Extensive fibrosis with marked round cell infiltration Slight necrosis and slight hemorrhage Reaction moderate and well localized

Rabbit 6 Ligation and Inversion (examined at 30 days) *Laboratory Gross*—Peritoneal surface smooth *Microscopic*—Moderate fibrosis No necrosis No hemorrhage Slight inflammation

Rabbit 7 Inversion without Ligation (examined at 48 hours) *Laboratory Gross*—Stump cleanly invaginated with mesentery adherent to site of invagination On section, there is an encapsulated hematoma in the stump *Microscopic*—Marked hemorrhage into the tissue with round cell infiltration along margins and considerable fibrosis with beginning organization No necrosis seen

Rabbit 8 Inversion without Ligation (examined at 7 days) *Laboratory Gross*—Inverted stump covered by fibrous adhesions No evidence of hemorrhage Feels like a hard fibrous nodule *Microscopic*—Marked fibrosis Slight inflammation One small area of stump necrotic No hemorrhage Slight reaction in tissue

Rabbit 9. Inversion without Ligation (examined at 30 days) *Laboratory Gross*—Peritoneal surface smooth No adhesions *Microscopic*—Slight fibrosis, no inflammation, no necrosis, no hemorrhage Slight reaction in tissue



FIG 3—(Rabbit 6)—Section treated by ligation and inversion, taken 30 days after operation

#### COMMENT

Emphasis has been placed on end results as determined by 30-day specimens Interval specimens of inversion of the stump, on microscopic examination revealed hemorrhagic infiltration Since this phenomena was not noted in unburied stump specimens treated by simple ligation ("tie and drop"



method), it was attributed to trauma associated by insertion of the purse-string suture. The danger of injury to blood vessels during insertion of the inverting purse-string suture was emphasized by Colf in 1926.

Buikle-de la Camp, in experiments on monkeys, Goode and Kregel on dogs, and Kloss on rabbits were able to demonstrate advantages of invagination of the unligated stump.



FIG 4—(Rabbit 9)—Section treated by inversion without ligation, taken 30 days after operation.

Kloss noted mesenteric lymph node enlargement constantly associated with stump inversion, and absence of this change when the stump was left unburied. In this series, no significant variation of lymphatic enlargement was noted.

In this study, many specimens revealed varying degrees of inflammation and necrosis. Encapsulated hematomas were not an infrequent phenomena. No specimen—either buried or unburied—revealed abscess formation—either macroscopically or microscopically.

Microscopically—the interval specimens revealed considerably more inflammatory reaction in the cecum in the buried stump than in the unburied, and more with the ligated buried stump, than when unligated and buried. This latter observation has been noted previously. It is probably

due to more adequate drainage by continuity of unligated, crushed, necrotic tissue through the residual lumen of stump, communicating with the lumen of the cecum.

Under pathologic conditions of inflammation associated with appendicitis this type of reaction would probably be much more exaggerated. Anatomic characteristics of the human cecal-appendiceal area offer greater protective advantages from the surgical viewpoint than noted in most experimental animals.

#### DISCUSSION

1—End results of the standard methods of treatment of the appendiceal stump (a) ligature or “tie and drop” method, (b) inversion into the wall of the cecum of either the ligated or unligated stump, as observed in this study, do not justify claims of the superiority of one method over the other.

2—Interval studies of the two methods revealed no gross discrepancy between the methods but did reveal greater microscopic inflammatory reaction

in the inversion technic This is probably secondary to trauma from insertion of the purse-string suture

3—Contamination, hemorrhage and inflammatory reaction would probably be greater with the purse-string suture method than with the simple ligature or "tie and drop" method, under conditions of infection and inflammation

#### CONCLUSION

Under controlled laboratory conditions and comparative technic, no superiority of any one method of treatment of the appendiceal stump, as determined by end results, could be demonstrated

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# TALCUM POWDER GRANULOMA A FREQUENT AND SERIOUS POSTOPERATIVE COMPLICATION\*

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THIS STUDY OF TALC GRANULOMA is being presented in order to stress the seriousness and frequency of a known postoperative complication and to suggest a way by which it may be prevented

During the past 14 years sporadic reports of talcum powder granulomas following surgical operations have appeared in the literature Because some of these reports have dealt with a small number of cases scattered over a long period of observation, many surgeons and pathologists have tended to consider the problem chiefly as one of academic interest During the period in which no apparent solution to the fundamental problem was in evidence there perhaps was some excuse for this attitude Now that alternatives to the use of this dangerous agent in the operating room are available, it is well to realize the variety and seriousness of the complications that may arise from the use of talcum powder on surgical gloves

This study reviews 37 cases of talcum powder granulomas producing symptoms serious enough to require admission to the Barnes Hospital for treatment In each instance a previous operation had resulted in the leaving of enough talcum powder in the wound to result in a severe silicotic reaction with consequent serious postoperative complications

Antopol<sup>1</sup> in 1933 was the first to call attention to the clinical and pathologic significance of Lycopodium and talcum powder granuloma in surgery He presented 6 cases of granuloma caused by Lycopodium spores and talcum powder crystals introduced into a surgical wound from the surgeon's glove He pointed out the clinical similarity of these lesions to both neoplasm and to tuberculosis

Erb<sup>3</sup> in 1935 reported 6 cases of talcum powder granuloma In 3 of these cases the granuloma was an incidental finding but in the other 3 patients, the talc granuloma was the fundamental cause of the postoperative complaints One of these cases had a severe talc reaction deep within the brain substance following a neurosurgic procedure

In 1936, one other case was reported by Owen<sup>12</sup> A year later Fienberg<sup>4</sup> reported five instances in which talc crystals were discovered in microscopic sections by the use of crossed Nicol prisms Birefringent material (of which talc is an example) will by this method of examination rotate a beam of polarized light The latter author reviewed 30,000 cases and states he found

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\* Read before the Meeting of the American Surgical Association, March 25-27 1947  
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FIG 1A

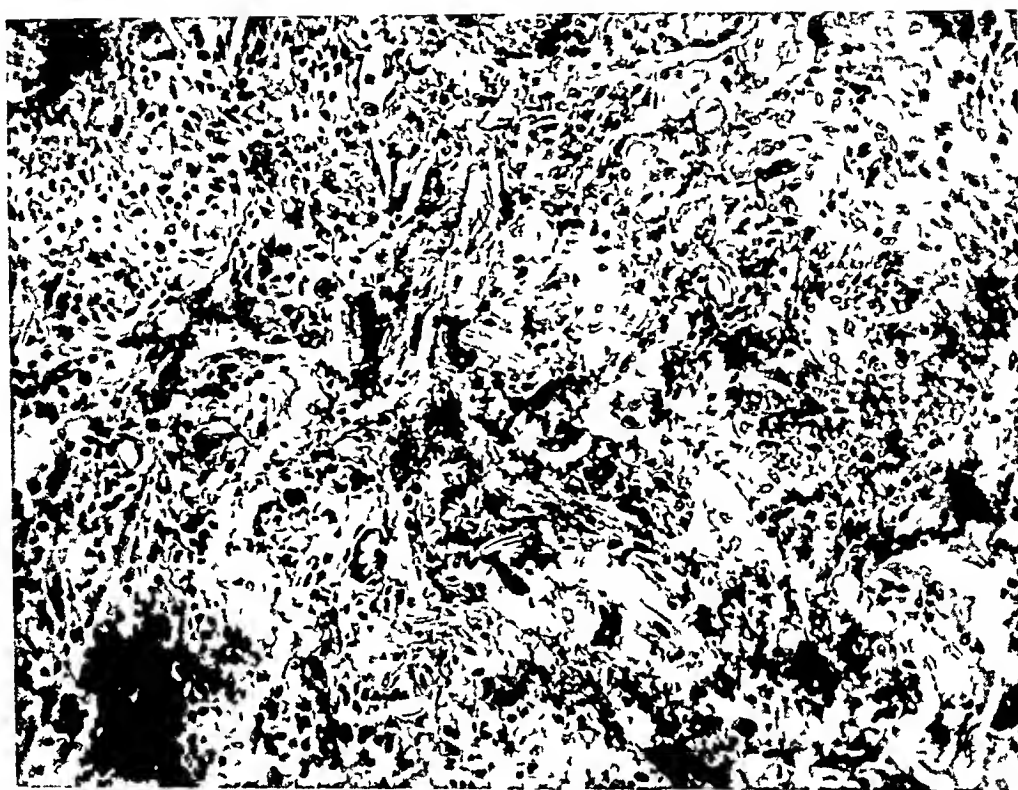


FIG 1B

FIG 1A—Talc granuloma in lumbosacral extradural space following laminectomy. The process is recent and there are numerous giant cells (H & E  $\times 150$ )

1B—Photograph of same field seen in FIG 1A taken with polarized light to demonstrate the massiveness of contamination ( $\times 150$ )

FIG 2A

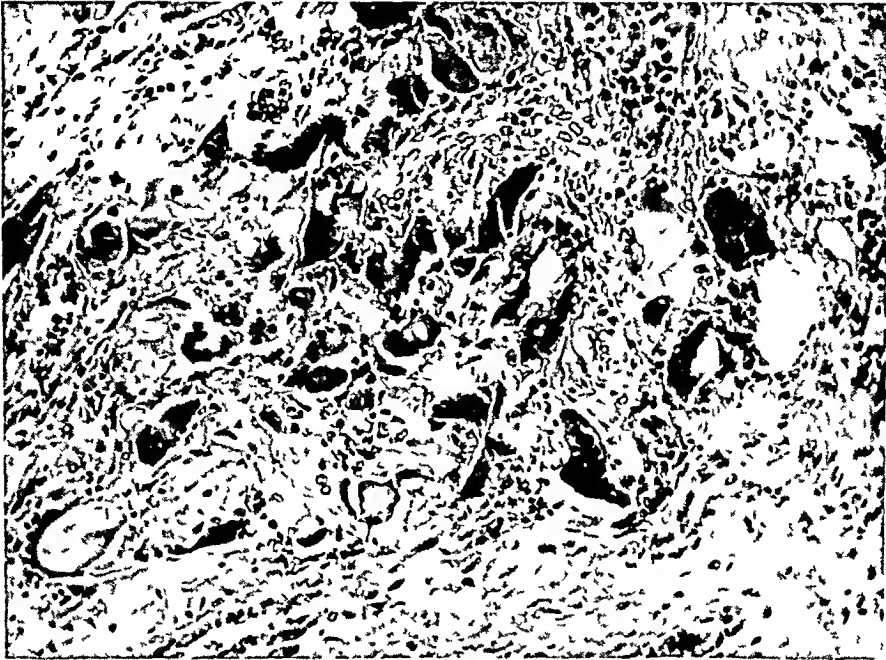


FIG 2B

FIG 2A—Active reaction to talc in the wall of the ileum following appendectomy. This had resulted in a persistent fecal fistula. The fibrosis around the giant cells is dense and had extended deep into the intestinal wall, where it was associated with secondary infection (H & E  $\times 150$ ).

2B—Photograph of same field seen in Fig 2A taken with polarized light to demonstrate the birefringent talc ( $\times 150$ ).

# TALCUM POWDER GRANULOMA

FIG 3A

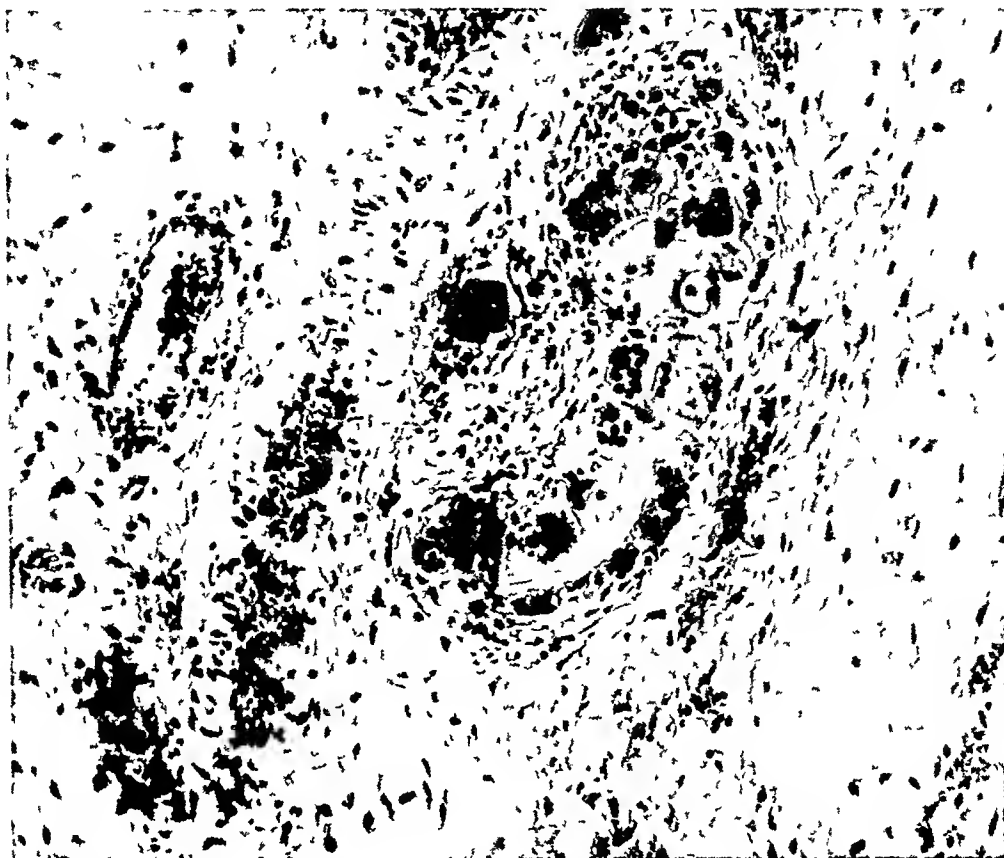


FIG 3B

FIG 3A—Reaction to an unusually large talc crystal. This followed appendectomy, and the resulting lesion was diagnosed roentgenologically and clinically as regional ileitis. There was a diffuse area of edema and fibrosis involving the terminal ileum (H & E  $\times 150$ ).

3B—Photograph of same field seen in FIG 3A taken with polarized light ( $\times 150$ ).

FIG 4A



FIG 4B

FIG 4A —Reaction to talc adherent to chromic catgut This was a peritoneal suture and resulted in the formation of adhesions with subsequent intestinal obstruction We have noted stenosis of enterostomy stoma as a result of such a reaction to talc contaminating suture material

FIG 4B —Photograph of same field seen in Fig 4A taken with polarized light to demonstrate widespread contamination with birefringent talc

but 5 examples of talc granuloma. He reviews, however, only those cases that had been diagnosed as foreign body reaction of an unknown type.

Grieco<sup>7</sup> in Italy reproduced talc granuloma in animals by injecting a fine suspension of talc crystals subcutaneously and intraperitoneally. He demonstrated that only a few crystals were required to incite a large mass of inflammatory reaction.

Ramsey and Douglass<sup>13</sup> in 1940 added 5 cases to the literature and cautioned against the use of talcum powder in the operating room. The same year German<sup>5</sup> noted the similarity between the reaction of the subcutaneous tissue to silica and that of the microscopic picture in sarcoid, pointing out that foreign body granulomas might well be confused with sarcoid.

Ten more cases were added to the literature in 1941 and 1942 when McCormick and Ramsey,<sup>11</sup> Byron and Welch,<sup>2</sup> and Ramsey<sup>14</sup> reported a variety of manifestations of this underlying granulomatous lesion. These authors noted the production of peritoneal granulomas, and of chronic draining sinuses caused by the seeding of talcum powder into the peritoneal cavity during various surgical procedures.

Weed and Groves<sup>21</sup> in an effort to find the mechanism of talcum powder contamination of wounds, studied surgical gloves after their operative use. They found that in 74.4 per cent of all operations at least one of the gloves used by the operating team was torn. Of all gloves examined 22.6 per cent showed perforation following use in the operating room. This work emphasizes the fact that simple washing of the gloved hand would not remove the danger of contaminating the surgical field with talcum powder. A relatively large amount of powder remains inside the glove and can easily be spilt into the wound when a glove is perforated.

German<sup>6</sup> in a subsequent report reviewed 20 cases in which he found upon microscopic examination large numbers of talc crystals within the tissue. He required 3 or more crystals per microscopic field before he would consider talc as a causative agent. From his animal experiments in the production of talc granuloma, he states that concomitant tissue trauma is necessary in the region of talc implantation for the production of granuloma.

Wells<sup>22</sup> in 1944 noted a number of cases in which talc granuloma had caused a failure of surgical wound healing.

A number of authors have thus recognized the dangers in the use of talcum powder. Seelig, Verda and Kidd<sup>17</sup> in 1943 were the first to offer a substitute for this offending material. They suggested the use of potassium bitartrate powder which they pointed out caused no such tissue reaction as did talc, and was relatively resistant to autoclaving. They also called attention to the bacteriostatic properties of this powder. Subsequent to their report, this material has been adopted by a number of surgeons throughout the country with varying success. The greatest drawback to the use of potassium bitartrate is that if autoclaved for longer than 20 minutes it tends to caramelize, making rubber gloves sticky as well as decreasing their elasticity.

Seelig<sup>18, 19, 20</sup> in a series of three papers in 1944 and the year following,



re-emphasized the dangers of talcum powder in the operating room, and offered another more desirable substitute in the form of a specially treated starch powder. It was felt that this new agent once available would replace both talcum powder and potassium bitartrate.

Recently Lichtman<sup>8, 9</sup> *et al* have published two papers reviewing the entire problem very thoroughly. They present a large series of lesions in which the reaction to talcum was considered to be an etiologic factor, and discuss the microscopic similarity between the talcum lesions, sarcoid and tuberculosis. They also point out the similarity between talcum powder granuloma and some of the manifestations of regional enteritis.

During recent years surgical specimens showing chronic inflammatory lesions have been examined by us with crossed Nicol prisms, and many clinically unsuspected cases of talcum powder reaction have been identified. The prevalence of these lesions and their varied clinical manifestations prompted us to review the surgical pathologic material at the Barnes Hospital in an effort to correlate our experience with this condition. Many cases coming to re-operation prior to the recognition of the propensities of talcum powder to cause such granuloma had been incorrectly diagnosed, only to be discovered upon re-examination in the light of later knowledge. It is interesting to note that in several cases the pathologist remarked upon the reaction as being "similar to one around a foreign body," but talc was not incriminated until after Antopol's article in 1933.

The fact that talc crystals are found in a microscopic section does not necessarily mean that they underly the essential nature of the pathologic lesion. A high percentage of cases at re-operation show evidence of the presence of a few talc crystals but in most cases they are merely an incidental finding. Crystals around the periphery of the section are felt to be contaminants, probably from the examining pathologist's glove. For this reason precipitated calcium carbonate is used as a dusting powder in the surgical pathologic laboratory, it being adequate as a powder and impossible to confuse with talc crystals because of the inability of chalk to rotate polarized light.

We have tried assiduously to avoid indicting talcum powder as the primary etiologic agent in a case until certain criteria have been fulfilled. These are:

- 1 The finding of doubly refractile crystals in the microscopic section. These crystals must be within the body of the material sectioned.
- 2 The crystals must have the morphology of talc, as differentiated from lint, fibers of cotton, silk, cholesterol crystals, etc.
- 3 A typical foreign body reaction must be present immediately around these crystals, which includes the presence of multinucleated giant cells, round cells, and a varying amount of vascular fibrous connective tissue.
- 4 Clinical interpretation consistent with talcum powder granuloma. This includes a previous operation at the site of granuloma formation, and no other evident source of origin to explain the condition.

Using these criteria 37 cases have been identified in which a reaction to

# TALCUM POWDER GRANULOMA

TABLE I

Case No	Original Operation	Time Between Orig Op and Appearance of Symptoms	Chief Complaint	No of Operations Subsequent	Operations Performed	Duration of Symptoms	Died
1	Appendectomy	3 wks	Intestinal obstruction	1	Lysis adhesions	6 wks	
2	Appendectomy	5 days	Abdominal sinus	5	I&D Curettings lap	2 yrs +	
3	Suprabic prostatectomy	0	Abdominal sinus	2	Curettings	2 mos	
4	Removal of wart	0	Scar on face	8	Plastic to face	2 yrs +	
5	Appendectomy	5 days	Abdominal sinus	2	Excision sinus	17 mos +	
6	Cholecystectomy	0	Abdominal sinus	2	Lap I & D	8 mos	
7	Salpingectomy, oophorectomy	5 days	Urinary and fecal fistula	3	Closure fistulae	10 yrs	
8	Myomectomy, appendectomy	0	Abdominal sinus	2	Excision sinus I&D	10 mos +	
9	Appendectomy	0	Abdominal sinus	1	Excision sinus	2 mos	
10	Appendectomy oophorectomy	9½ yrs 6 days	Fecal fistula	2	Closure fistula	6 mos	
11	Laparotomy	0	Abdominal sinus	2	Lysis adhesions	6 mos	
12	Appendectomy	5 mos	Mass in RLQ	1	I & D abscess	1 mo	
13	Appendectomy	0	Fecal fistula	4	I&D, excision sinus, resection	1 yr	
14	Appendectomy	3 wks	Abdominal sinus	3	Excision sinus	2 yrs	
15	Herniorrhaphy	0	Mass sinus	2	I & D	3 yrs	
16	Appendectomy	0	Fecal fistula	3	Closure fistula	21 yrs	
17	Laparotomy	3 mos	Intestinal obstruction	6	Lysis adhesions, colostomy, resection ileum	3 yrs	
18	Appendectomy	3 mos	Abdominal sinus	2	Excision sinus	6 mos	
19	Appendectomy	14 mos	Abdominal sinus	4	I&D curettings	2 yrs	
20	Appendectomy	0	Abdominal sinus	4	Laparotomies exploration	26 mos	
21	Nephrectomy	2 mos	Lumbar sinus	1	Excision sinus	2 yrs	
22	Appendectomy	7 mos	Mass in RLQ	2	I & D	20 mos +	
23	Appendectomy	0	Abdominal sinus	3	Lysis adhesions I&D	7 mos +	
24	Appendectomy	0	Intestinal obstruction	5	Lysis adhesions, ilectomy	3 yrs +	
25	Gastrectomy	1 mo	Obstruction anastomosis	5	Esophagoplasty, lysis adhesions	6 mos	
26	Abdominal hysterectomy	1 wk	Fecal fistula	2	Ileocecostomy closure	3 mos	X
27	Laminectomy	2 mos	Sinus	1	Excision sinus	6 mos	
28	Laparotomy	1 yr	Intestinal obstruction	3	Ileostomy resection		
29	Laparotomy	1 wk	Abdominal sinus	3	I & D	6 mos	
30	Appendectomy	2 mos	Intestinal obstruction	3	Lysis adhesions resections	6 mos	X
31	Thoracotomy	0	Chest sinus	2	Curetting sinus	10 mos	
32	Appendectomy	10 yrs	Intestinal obstruction	3	Lysis adhesions, enterostomy	11 yrs	
33	Abdominoperineal resection	2 yrs	Stenosis colostomy	1	Enlargement colostomy stoma	6 mos	
34	Laminectomy	0	Pain in leg	1	Laminectomy excision granuloma	13 mos	
35	Abdominoperineal resection		Stenosis colostomy	1	Enlargement colostomy stoma		
36	Cholecystectomy	0	Intestinal obstruction	3	Lysis adhesions	2 yrs	
37	I&D perineal abscess	0	Perineal sinus	2	Excision perineal sinus	2 mos	

talcum powder produced the essential lesion Table I summarizes the important data of these cases

Not included in this series is a considerably larger group in which all of the criteria mentioned above could not be satisfied In this latter group the majority of the patients had undergone previous laparotomies with resulting dense diffuse adhesions As can be noted in the photomicrographs, a minute amount of talc is capable of producing a wide fibrotic reaction The cellular reaction in these cases was identical with that resulting from talc, but because sufficient amount of talc could not be identified, we have not felt justified in including them in the present series We call attention to them, however, to stress the point that the talc reaction in our opinion plays a prominent role in many instances in the formation of that type of dense stenosing fibrosis so often associated with postoperative symptoms

The most striking fact concerning this group of postoperative patients is the diversity of the clinical syndromes that they represent The most common finding is that of a surgical wound that failed to heal postoperatively Twenty-three cases (62 per cent) had such a manifestation 15 had a chronic abdominal sinus, 1 a lumbar sinus, 1 a sinus in the chest wall, and 1 a perineal sinus A few of these were simple superficial wounds and were considered clinically to be stitch abscesses Others extended deep into the peritoneal cavity

Besides these sinuses, five fecal fistulas were found Before including these cases, ample evidence of talc deep in the sinus wall was required, for many doubly refractile vegetable bodies could pass into such a fistulous tract from the lumen of the intestine As in Lichtman's series<sup>8</sup> many of these cases with fecal fistulae had been thought clinically to have regional enteritis

Table II shows the frequency of the various clinical complaints

TABLE II  
CLINICAL COMPLAINTS IN 37 PATIENTS WITH POSTOPERATIVE  
TALCUM POWDER GRANULOMA

Sinus	18
Abdominal sinus	15
Lumbar sinus	1
Chest sinus	1
Perineal sinus	1
Fecal fistula	5
Intestinal obstruction	7
Tumor mass	3
Neurologic signs	2
Stenosis	2

Most of the patients in this series had many previous operative procedures before being seen in this hospital Eight patients (22 per cent) had four or more operations The average patient had 2.5 operations with no assurance that more procedures would not be required after discharge In two patients further surgery is known to have been performed at other hospitals when emergency procedures were necessary

The type of operation performed in treating these complaints were varied

Seventeen patients had closure or attempted closure of a chronically draining sinus. Many of these patients required multiple operations. Lysis of post-operative intestinal adhesions was carried out in seven cases, and a like number required bowel resection. Incision and drainage, with curettage of sinuses was performed in 21 cases.

The condition most often confused with talc granuloma clinically in this series was tuberculosis. This was due to the chronicity of the signs and symptoms and to the similarity in the gross between the granulomatous lesions. Non-caseous tuberculosis was a repeated suggestion in the clinical histories, and gross examination often lent weight to the diagnosis. The microscopic picture was of course always slightly atypical of tuberculous infection.

As previously noted, regional enteritis was often suggested when small bowel symptoms predominated.

Talc granuloma is a chronic condition. In this series, symptoms ranged from a few months to 21 years. During this time there were long silent periods in which no evidence of foreign body was seen. Then without obvious stimulus there were symptoms of irritation. Although a few cases had their first symptoms occur in a matter of months after operation, most had some evidence of foreign body reaction during their immediate postoperative hospital stay. Those cases with obstructing intestinal adhesive bands seemed to have late evidence of their talc reaction, perhaps because it required some time for the adhesions to form and become constrictive.

There were two deaths in this series.

The primary operations during which time talc was implanted represent procedures in all branches of surgery and its specialties. The most common operation responsible for talc spillage was appendectomy (49 per cent), followed by laparotomy for unknown procedures (11 per cent). Gynecologic operations accounted for 11 per cent of the cases, genitourinary, orthopedic, plastic, thoracic and neurosurgical procedures each were responsible for at least one example of talc spillage and subsequent reaction.

The danger of this silicotic reaction, therefore, is universal. In some areas small granulomas may cause fewer symptoms than others. This proliferative process once present usually persists for years. The part it plays in the production of postoperative abdominal adhesions has been tragic and apparent. The damage in other surgical procedures such as craniotomy, while present, has been less obvious.

#### PATHOLOGY

Upon gross examination talc granulomas are not pathognomonic. In cases where a mass was observed, the operative notes almost invariably mention the hard consistency and pearly white or grey color of the tumor. In many cases biopsy of the area was made upon laparotomy because of the dense consistency of the area, which suggested malignancy. When small multiple, discrete areas of reaction were seen at operation, the surgeon's note often mentions the resemblance to miliary tubercle formation. Adhesive bands within the peritoneum were noteworthy because of their dense inelastic consistency and

their vascularity The pathologist usually described the smaller lesions as feeling shotty when rolled between the fingers

The largest granuloma in this series was a sausage shaped mass involving the transverse colon, measuring 14 cm in length and 8 cm in width (Case No 30) Most of the granulomas, however, were small nodules measuring about 1 cm in diameter

Microscopically talc granuloma fits in with those agents that upon introduction into the body cause a foreign body reaction of the proliferative type<sup>10</sup> Pulmonary silicosis has been widely studied, and talc (Magnesium Silicate) reaction is merely a localized form of this same condition

Talc crystals are seen microscopically to be surrounded by masses of fibrous tissue in which there is excessive collagen production along with inflammatory cells Individual talc crystals are seen to be the nidus of the inflammatory reaction, which has a peculiarly wild and unoriented appearance Connective tissue strands are mixed in whorls and cross currents as they envelop the irritating talc particles The cellular response consists of foreign body giant cells which surround (and in the case of small crystals also ingest) the talc particles No evidence of destruction of these non-absorbable particles is seen so that the reaction by no means resolves the condition The multinucleated cells in some cases reach tremendous proportions, generally with a clear cytoplasm in which numbers of small nuclei are eccentrically clustered Small round cells are typically in evidence No caseation is ever seen

The microscopic similarity to a tubercle is evident, for a focus of inflammatory reaction is surrounded by lymphocytes, giant cells, and a proliferative connective tissue response Identification of talc crystals in the center of the lesions is of course the point of differentiation This can be performed on routine examination merely by using a strip of polaroid material between the light source and the microscopic slide, and another such polarizing strip between the slide and the eye arranged so as to darken all but birefringent particles

Foreign body reactions from other materials are often similar microscopically to that due to talcum powder crystals The reaction to suture material is of interest in this respect Strands of cotton or silk are themselves slightly birefringent It was noticed in several cases, however, that strands of such sutures were surrounded by a halo of birefringent particles that did not appear to be silk or cotton fibers, but rather to be of the nature of talcum powder crystals For this reason, several sutures were mounted on a slide and examined with polarized light It was found that sutures that were new and dry showed none of these birefringent particles Suture material from the same source was then wet in water and run through a hand that had been dusted with talcum powder The particles of talc obviously were transferred to the wet suture, and became adherent It is possible, therefore, that much of the foreign body reaction ascribed to suture material may actually be due to the tiny talc particles that are adherent to the thread

From our own experience and from that of others where talcum powder

is used on the hands and gloves or where it is on the scrub nurse's table it is a source of danger. The deposition of a thin layer of talc on gauze sponges, packs, and on the instruments follows the all too frequent and vigorous powdering of the hands preparatory to donning gloves. With care this hazard may be lowered, but even the utilization of utmost care cannot completely exclude the possibility of occasional accidental contamination.

The ability of talc to spread throughout a room can easily be demonstrated by placing a dark piece of paper or a book on one side of the room, then carefully powdering the hands on the opposite side of the room. In a matter of a few minutes a thin layer of talc will be seen settling on the darkened surface.

It would seem to us that the best answer to the problem is either the use of wet gloves or the substitution of an innocuous dusting powder. As previously mentioned, potassium bitartrate has been used as such a substitute. More recently, starch treated with formaldehyde in order to prevent the formation of a gel upon autoclaving has been tried. Seelig has shown the lack of tissue reaction to this material in a series of elaborate animal experiments.

Various treated starch compounds have been introduced into many animals (dogs, mice, rats, and guinea pigs). In no case does the powder elicit a granulomatous response. The innocuousness of starch in the tissue and the rapid rate of its dissolution is clearly evident when the powder is injected into the anterior chamber of a rabbit's eye. Examination of an animal four days after 2 mg of formalized starch has been introduced into the right eye, and 2 mg of talc had been injected into the anterior chamber of the left eye shows that starch has been absorbed, leaving no reaction. Severe fibrosis and tissue reaction is seen, on the other hand, in the talcum treated eye. The talc reaction subsequently caused blindness.

Unfortunately, however, very recent clinical experience has disclosed an unexpected difficulty. The formaldehyde starch is somewhat unstable, and seems to split up on ageing, liberating free aldehyde. This, of course, can act as an irritant to the hands of the surgeon. One corporation interested in developing the new powder seems to have used other aldehydes, and to have added magnesium carbonate to increase the "flow" of the powder. We have found previously that magnesium carbonate produces granulomata, moreover, the new aldehyde-starch powder has evoked hand irritation in one of our resident surgeons.

As a result of the more recent experience, we are still searching for an adequate substitute for talcum. More time must elapse before we can be sure that the aldehyde treated starch is completely innocuous to both the patient and the surgeon. In the meantime, as previously stated, potassium bitartrate, properly sterilized, can be used. Talcum must be banned from the field of surgery.

#### SUMMARY

1. Thirty-seven cases of postoperative complication due to talcum powder granuloma have been presented.

2 These cases represent a wide diversity of complications, ranging from simple wound abscesses to serious sequelae such as fecal fistulae and intestinal obstruction

3 The clinical and pathologic nature of this condition has been discussed

4 Emphasis has been placed upon the requirements of a suitable alternative dusting powder for use in the operating room

5 Review of our experimental and clinical trials of formalized starch compounds as dusting agents in the operating room has been given

6 The starch compounds as now produced are not completely stable, and must be further modified before we recommend their use

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# A SUSPENSION OPERATION FOR PROLAPSE OF THE RECTUM\*

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THE MULTIPLICITY OF OPERATIONS which have been described for the treatment of complete prolapse of the rectum is evidence that an operation has not yet been designed which can be considered entirely satisfactory. The principles involved in the various operations described are, (1) excision of the protruding bowel, (2) operations to reduce the size of the anus and lower rectum, (3) plastic operations to restore or strengthen the pelvic floor, (4) abdominal suspension, fixation, or both, of the prolapsed bowel, and (5) obliteration of the deep cul-de-sac.

The fact that the etiology of complete rectal prolapse is not entirely clear may have influenced the trial of many operative procedures without sound fundamental reasons. Complete rectal prolapse is probably primarily the result of an abnormally loosely attached rectum, a developmental defect, as suggested by Pemberton and Stalker.<sup>1</sup> These authors compare prolapse of the rectum to prolapse of the sigmoid following sigmoidostomy, when the sigmoid has a long mesentery. In addition to the loosely attached rectum, a deep cul-de-sac is present, which, due to intra-abdominal pressure, acts as a potential hernia between the rectum and vagina in the female, or rectum and bladder in the male (Moschcowitz).<sup>2</sup> Graham<sup>3</sup> interprets the prolapse as a sliding hernia of the anterior rectal wall through the anal canal. The natural defect in the pelvic fascia which permits the passage of the rectum through the diaphragm is enlarged by the pressure against the anterior wall of the contents of the cul-de-sac of Douglas. With enlargement of the normal outlet of the rectum and defective and lengthened supporting structures of the rectum, prolapse may be expected to occur.

If the cause of rectal prolapse is due to an abnormally attached recto-sigmoid with a long mesentery, and a deep cul-de-sac predisposing to hernia, an operation designed to correct these two anomalies should produce a cure.

## TECHNIC OF OPERATION (Figs. 1, 2, 3, 4)

Two strips of fascia 1 to 2 cm. wide and 10 to 12 cm. long are excised from the fascia lata.

A left paramedian incision is made from the pubes to a point about 2 cm. above the umbilicus. The patient is placed in the Trendelenburg position and the abdominal contents are packed away from the pelvis with warm moist pads. A tape is passed through the mesentery beneath the lower sigmoid for traction. Gentle traction will hold the prolapsed recto-sigmoid in normal position.

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\* Presented at the meeting of the American Surgical Association in Hot Springs, Virginia, March 25, 1947.



The fascia just above the promontory of the sacrum is exposed through an inverted T-shaped incision in the peritoneum. A strip of fascia is sutured to each side of the rectum with a double row of interrupted sutures of fine silk. The strip of fascia on the left is passed through a puncture wound made in the mesentery of the sigmoid. While the rectum is held suspended, the upper ends of the fascial strips are sutured to the dense fascia above the promontory of the sacrum. Interrupted silk sutures are used to attach both margins of the fascial strips to the fascia, a distance of at least 2 cm.

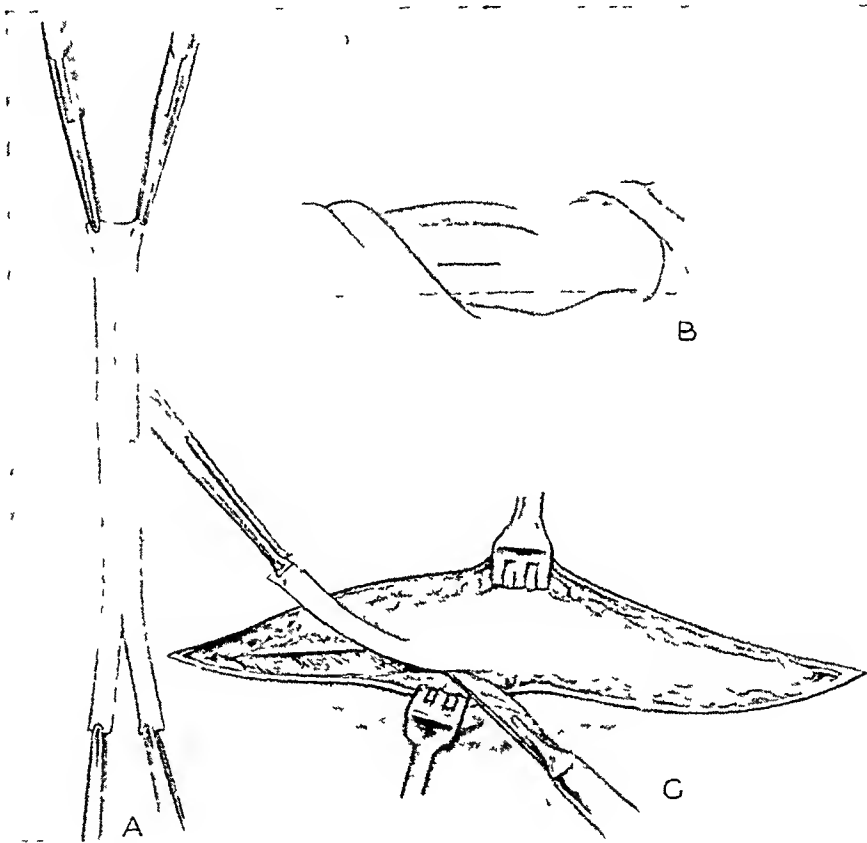


FIG 1—A, B, C Technic of removal of fascial strips from fascia lata

The cul-de-sac is completely obliterated by two or more rows of interrupted silk sutures placed across the pelvis. The peritoneum is sutured to the anterior wall of the rectum as each row of sutures is placed.

The pelvic operation is completed by suturing a fold of peritoneum to the rectum on each side to cover the fascial strips.

The abdominal and thigh wounds are closed with silk.

#### SUMMARY OF CASE REPORTS

**Case 1**—F. H., a male, aged 36, was admitted to the University of Kansas Hospitals February 18, 1941. He dates his illness following a fall from a horse about five

## PROLAPSE OF RECTUM

years before admission. His rectum began to protrude with each bowel movement. Examination showed a complete rectal prolapse about 10 cm in length. He was operated upon February 22, 1941. He made a good recovery and left the hospital on the 15th postoperative day. He last reported January 27, 1947. He has had no recurrence of the prolapse but has recently been constipated and complains of stomach trouble.

**Case 2—J A**, a male, aged 68, entered the hospital February 22, 1944. The first prolapse of the rectum occurred four weeks before admission. From the onset, the bowel

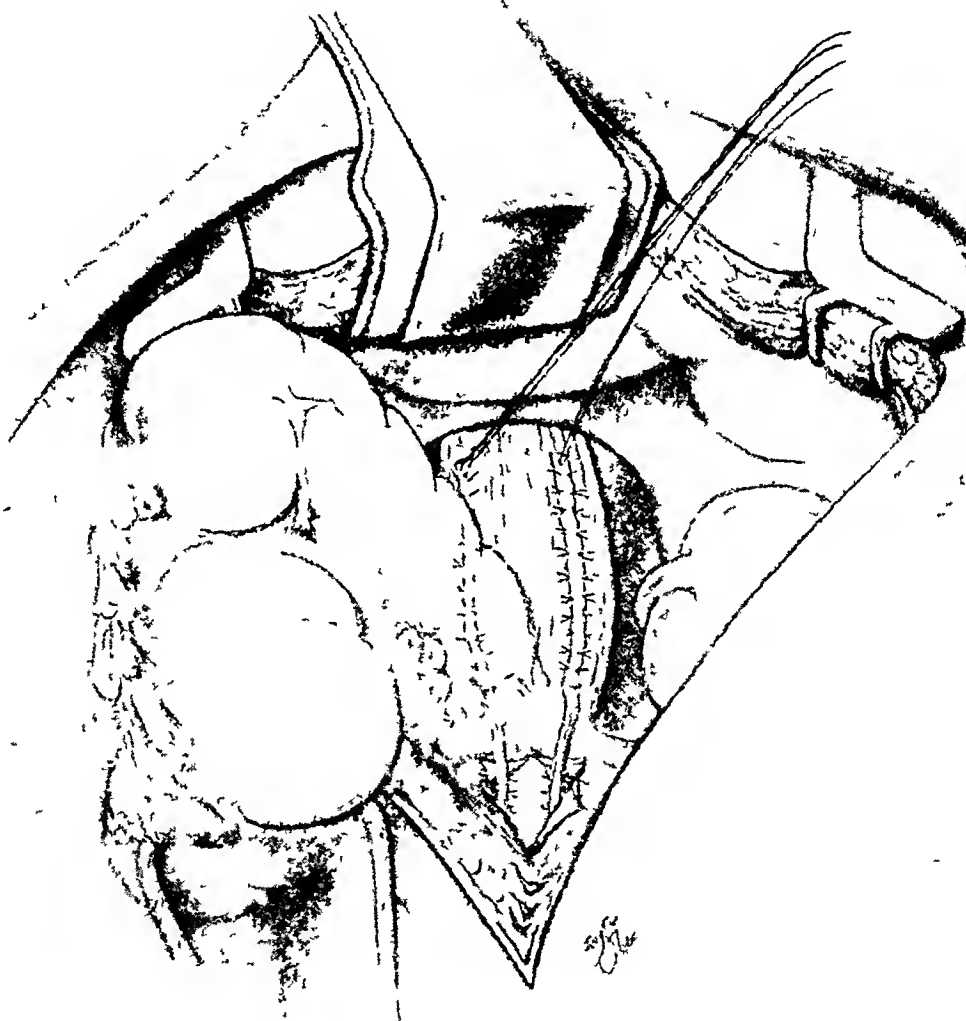


FIG 2—Fascial strips sutured to rectal wall and to fascia above the promontory of the sacrum. On the left the fascial strip is passed through the mesentery of the sigmoid.

prolapsed when his bowels moved and when standing. There had been some incontinence. This patient had a fracture of his spine one year before admission which resulted in spastic paraplegia. When straining the rectum protruded 5 to 10 cm. Since operation March 2, 1944, he has had no further evidence of prolapse. Because of his disability due to paraplegia he now spends much of his time in bed in a county institution. His condition was reported good on December 3, 1946.

**Case 3—J J**, a male, aged 33, entered the hospital November 12, 1945, complaining of rectal trouble. He had had a prolapse of the rectum at times since early childhood.

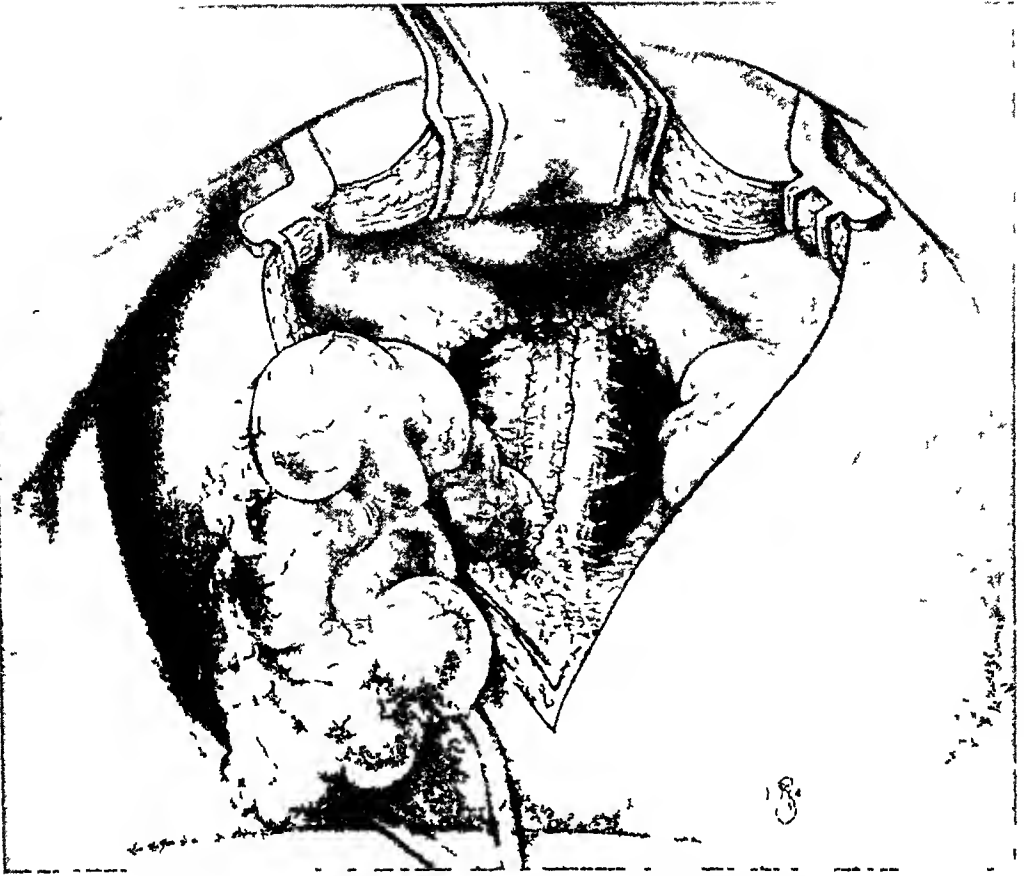


FIG 3—A fold of peritoneum has been sutured to the rectal wall on each side to cover the fascial strips. The cul-de-sac has been obliterated by rows of sutures placed transversely across the pelvis.

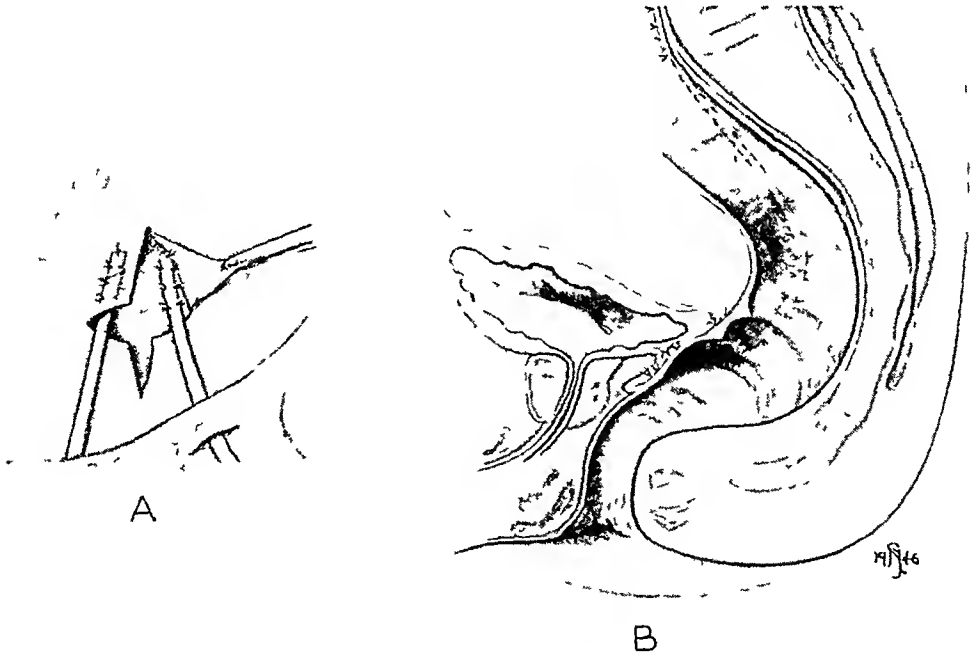


FIG 4—A Detail of attachment of fascial strips to fascia above the promontory of the sacrum.  
B Lateral view of pelvis showing closure of cul-de-sac and location of fascial strip on wall of rectum.

## PROLAPSE OF RECTUM

About two years ago he had some type of rectal operation without benefit. The prolapse was greater after the operation and was associated with a dull pain in the rectal region. Examination showed a complete prolapse of the rectum which could be reduced manually. He was operated upon November 14, 1945. He reported on December 6, 1946, that he has no rectal trouble but does have some discomfort in the lumbar region.

**Case 4**—Mrs. E. B., aged 66, was admitted to the Hospital on January 5, 1947. Prolapse of the rectum appeared about 15 months prior to admission. A rectal operation was done in February, 1946, which gave temporary relief. Asthma, which she has had several years, grew worse and she thinks persistent coughing may have influenced the return of the prolapse. For five or six months the prolapse grew worse until the rectum protruded constantly. She was a small emaciated woman weighing 84 pounds. The rectum protruded 10 to 12 cm. There was marked relaxation of the sphincters with almost complete incontinence. Following the operation on January 9, 1946, she made a good recovery and left the Hospital on the 12th postoperative day. On discharge she still had anal incontinence and some diarrhea. On March 15, 1947, her physician reported that there has been no recurrence of the prolapse and the sphincter tone has much improved. She has gained weight and is doing her housework.

TABLE I

Patient	Sex	Age	Date of Operation	Last Report	Result
F. H.	M	36	Feb. 22, 41	Jan. 27, 47	No recurrence of prolapse. Some constipation.
J. A.	M	68	Mar. 2, 44	Dec. 3, 46	No recurrence of prolapse. Condition good.
J. J.	M	33	Nov. 14, 45	Dec. 6, 46	No recurrence of prolapse. Some discomfort in back.
E. B.	F	66	Jan. 7, 47	Mar. 15, 47	No recurrence of prolapse. Sphincter tone improving. Doing own housework.

## RESULTS

The results in the four cases here recorded have been satisfactory to date (Table I). There has been no evidence of recurrence of the prolapse and the function of the rectum has been normal. The possibility of constriction or angulation of the lower sigmoid at the sacral promontory was considered but this has not happened. A barium enema has shown normal caliber of the rectosigmoid in two cases.

## CONCLUSIONS

A suspension operation for complete prolapse of the rectum is described.

The steps in the operation suspend the rectosigmoid from the fascia above the promontory of the sacrum with fascial strips and obliterate the deep cul-de-sac of Douglas. It is believed that suspension of the loosely attached rectosigmoid directly prevents prolapse through the anus and obliteration of the deep cul-de-sac eliminates a potential hernia which is a contributing factor in rectal prolapse.

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DISCUSSION—DR ROSCOE R GRAHAM, Toronto, Ont I should like to show four slides which have previously been presented before this Association They confirm the hypothesis which Doctor Orr has enunciated, namely, that in massive rectal prolapse the apex of the prolapse is the pelvic cul-de-sac In a patient with massive prolapse, the major portion of the visible bulge occurs at the expense of the anterior rectal wall as shown in Figure 1

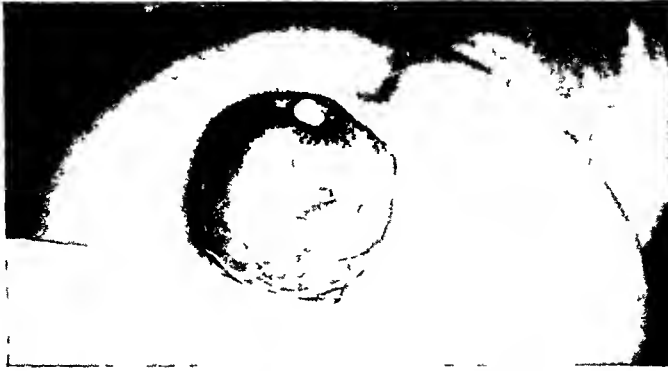


FIG 1—Patient in knee-chest position, with cork in lumen of rectum Shows the prolapse at the expense of the anterior wall

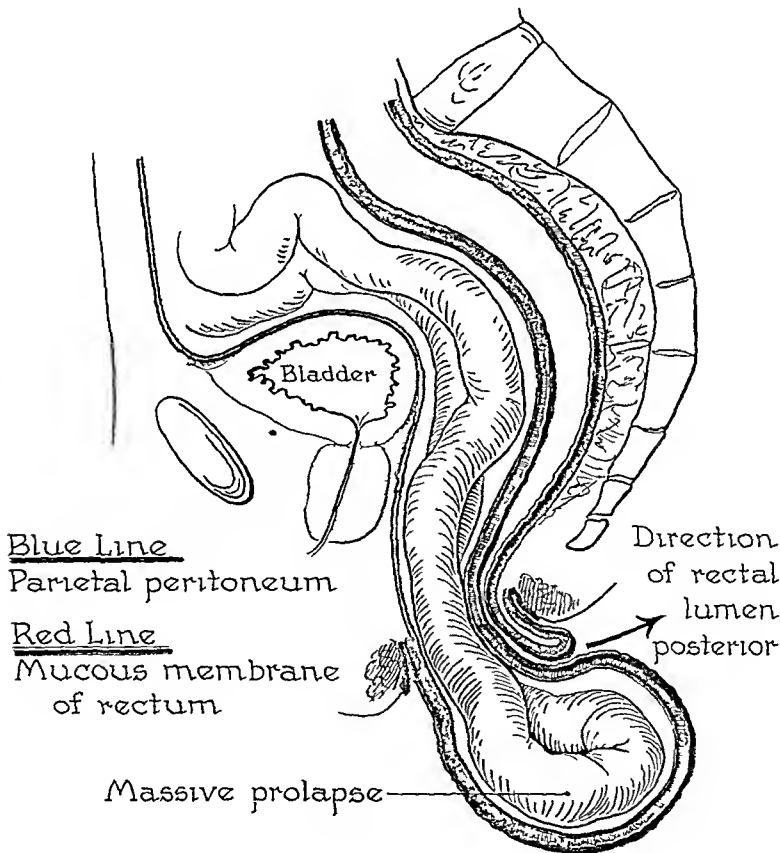


FIG 2—This shows very graphically the descent of the peritoneum at the expense of the anterior portion, and also demonstrates the eversion of the rectal mucosa through the sphincter

# PROLAPSE OF RECTUM



Fig 3—This shows the ureters isolated the medial margins of the levator grasped with sutures to place the rectum back in the hollow of the sacrum

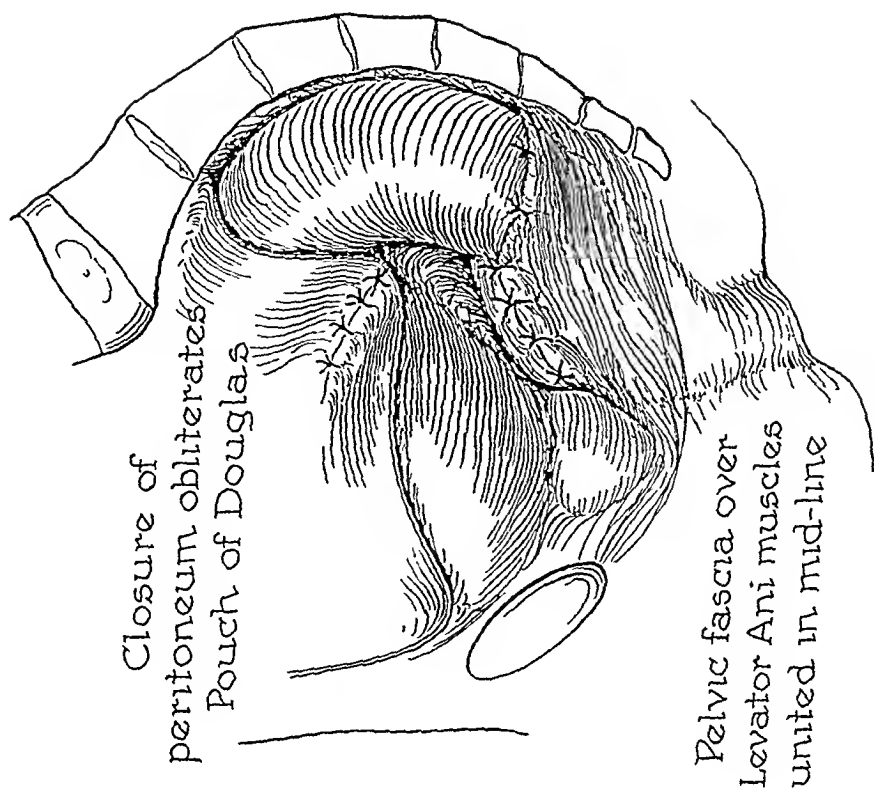


Fig 4—This shows the completed repair of the pelvic floor

The cork is placed in the lumen of the bowel and, with the patient in the knee-chest position, the major portion of the bowel lies anteriorly. This is well illustrated in Figure II. The blue line illustrates the parietal peritoneum, which has slipped down between the two levator ani as it gradually deepens the cul-de-sac, and shows that the direction of the rectal lumen is definitely posterior. Our conception of this mechanism is that the prolapse occurs through the separation of the levator ani muscles.

In Figure III the peritoneal cul-de-sac has been drawn up into the abdomen and separated, the ureters isolated, and one can then visualize the median margins of the two levator muscles. They are then approximated by interrupted sutures and this changes the course of the rectum, in which it is placed back in the hollow of the sacrum, as seen in Figure IV. When this suture line had been completed it was no longer possible to invaginate the anterior rectal wall through the anal orifice. We had changed the direction of force exerted through increased intraperitoneal pressure.

We have had three cases in which this has been carried out with success, now sufficiently long to feel that it is permanent, and my colleagues have carried out three more, and in these there has been no recurrence.



## LETTER TO THE EDITOR

Sir

The article of Womack and Crider, "The Persistence of Symptoms Following Cholecystectomy," on page 31 in the July, 1947, number of the *ANNALS OF SURGERY* gives an ingenious and hitherto ignored reason for some of the residual symptoms in cholecystectomized patients. The abundance of autonomic nerve fibers and their involvement in scar-tissue was well demonstrated in their histologic sections.

For some time I have regarded and treated the so-called "adhesions" after laparotomy as being due to minor causalgic states in which partially damaged afferent nerve fibers set up reflex phenomena, just as they do in the extremities. It is furthermore fairly well established that visceral pain in the upper abdomen is mediated by the splanchnic nerves, in the case of the biliary tract in the right splanchnic. Doctor Walter and I have recently reported relief of intractable pain due to calcareous pancreatitis following splanchnic nerve section. We also observed a calcareous biliary tract disease exhibiting a painless course after splanchnic nerve section. Recently we have injected paravertebral procaine from D<sub>6</sub> to D<sub>10</sub> on the right in a patient with persistent pain after cholecystectomy. She remained free of pain for six weeks after the first injection, and a second injection kept her symptom-free for another three weeks.

The purpose of this letter is to suggest that instead of excising multiple neuromata around the cystic and common duct and stripping them from their afferent fibers, one might consider temporary or permanent sympathetic interruption. One wonders whether the local excision of such trigger-zones as Womack and Crider suggest, will not be followed at a later date by a recurrence of fibrosis and a regeneration of nerve-fibers. Certainly splanchnic nerve section is followed by a degeneration of fibers clear into the Pacinian bodies (Sheehan 1933).

Sincerely yours,

*G De Takats, M D, Chicago*

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## RESTORATIVE ENDOANEURYSMORRHAPHY BY VEIN GRAFT INLAY\*

ARTHUR H. BLAKEMORE, M D

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IT WAS NEARLY FIFTY YEARS AGO that Dr Rudolph Matas<sup>1</sup> introduced the surgical terms restorative and reconstructive endoaneurysmorrhaphy. More than 50 years have elapsed since he demonstrated to the profession that gangrene may be regularly avoided by employing his technic of obliterative endoaneurysmorrhaphy for the cure of aneurysm of the extremities. Though Doctor Matas early recognized the advantage of maintaining a pulsating arterial blood flow to the affected extremity for a complete restitution of function, his restorative technic clearly demonstrates that the attempt is made not at the expense of important collateral vessels—the salient feature of all his technics is the preservation of collateral vessels through an intra-saccular approach.

It is my wish to present a technic of vein graft inlay for the repair of degenerative arterial aneurysm with restoration of blood flow which conserves the principle of minimal damage to collateral vessels.

### METHOD

A generous skin incision affording free access to the proximal and distal poles of the aneurysm is made, the edges of the skin are covered with towels held in place by Michel clips. Following the securing of hemostasis, gloves and instruments are changed before proceeding with the operation. Time may be conserved by having an assistant proceed with the removal of a segment of vein for use as a graft—preferably from another extremity. The superficial femoral vein is most commonly used. An incision of the fascia is made directly over the aneurysm. The afferent artery can usually be located by palpating the pulse and identified by blunt dissection staying close to the upper pole of the aneurysm sac. A double turn of vaselined umbilical tape serves well for temporary occlusion of the artery. Should a sizable collateral branch arise at or very near the artery-aneurysm junction, this may be separately

\* Read before the American Surgical Association, March 25, 26 and 27, Hot Springs, Virginia.



controlled with a double turn of heavy silk. The efferent parent artery is likewise identified and controlled.

The aneurysm sac is then opened widely from pole to pole following securing of the parent artery by tapes or rubber shod clamps. The clot is quickly evacuated and a search is made for the openings of vessels within the sac. All vessel openings exclusive of the parent artery openings are sutured with three zero Deknatel silk from within the sac. Next, the distance between the parent artery openings within the sac is measured. To this measurement add four centimeters for the correct length of the vein graft to be used to bridge the arterial defect.

Vitalium tubes, as recommended in a non-suture method for vein graft bridging of arterial defects<sup>2</sup> serve as a prosthesis for retention of the vein graft inlay. Figure 1 illustrates the vitalium tubes and the method of mounting a tube on either end of the vein graft<sup>4, 5, 6</sup>. The everted vein is held in place by a four zero Deknatel silk ligature placed around the tube behind a tying (holding) ridge on the tube.

Figure 2A illustrates an aneurysm with the sac open to show the parent artery openings. Two smaller openings are likewise indicated. Rubber shod clamps to control blood flow are illustrated. The size of the openings of the parent artery indicate the size of the vitalium tubes to be employed. In some cases of large aneurysm the openings are far apart and it may be necessary to employ a vitalium tube one millimeter smaller for the distal opening. On the other hand, it is fortunate that usually the openings are larger in diameter than the parent artery. This enables the operator to introduce with ease larger vein mounted tubes than would be possible if the parent artery were severed from the aneurysm.

Figure 2B illustrates the vein graft inlay in place. The retaining sutures of zero Deknatel silk are placed around the vein mounted vitalium tubes so that when tied tightly with a surgeon's knot the ligature falls behind the holding ridges on the tubes. The sutures of finer (three zero) Deknatel silk placed near the ends of the vitalium tubes are tied, just snug, to coapt the vein and artery intimas. Some care must be employed both in the accurate placement of these sutures and the avoidance of a contiguous nerve or vein in case, as sometimes happens, part of the suture may be extra-saccular.

On account of vein valves, the proximal end of the vein graft should, of course, be joined with the distal artery opening.

Figure 2C shows the retaining ligatures tied, the parent artery deoccluded and sutures placed in the sac wall which, when tied, will cover the vein graft. It is important at this stage of the operation to make sure that any air bubbles within the vein graft are made to pass on by pressure upon the graft or elevation of the extremity.

Figure 2D illustrates the vein graft covered and additional sutures placed for imbricating the aneurysm sac. Silk technic is employed throughout and the wound is closed without drainage.

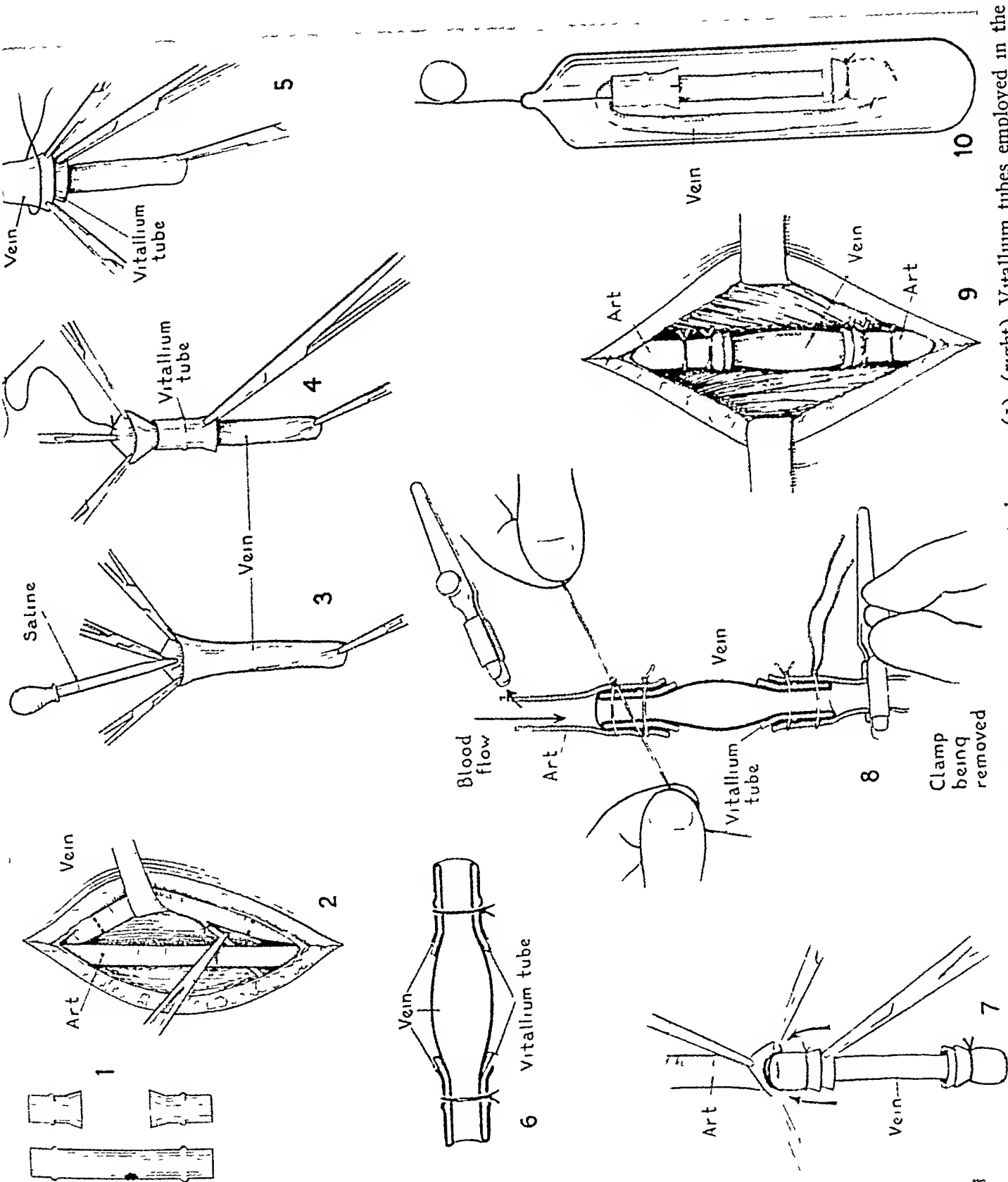
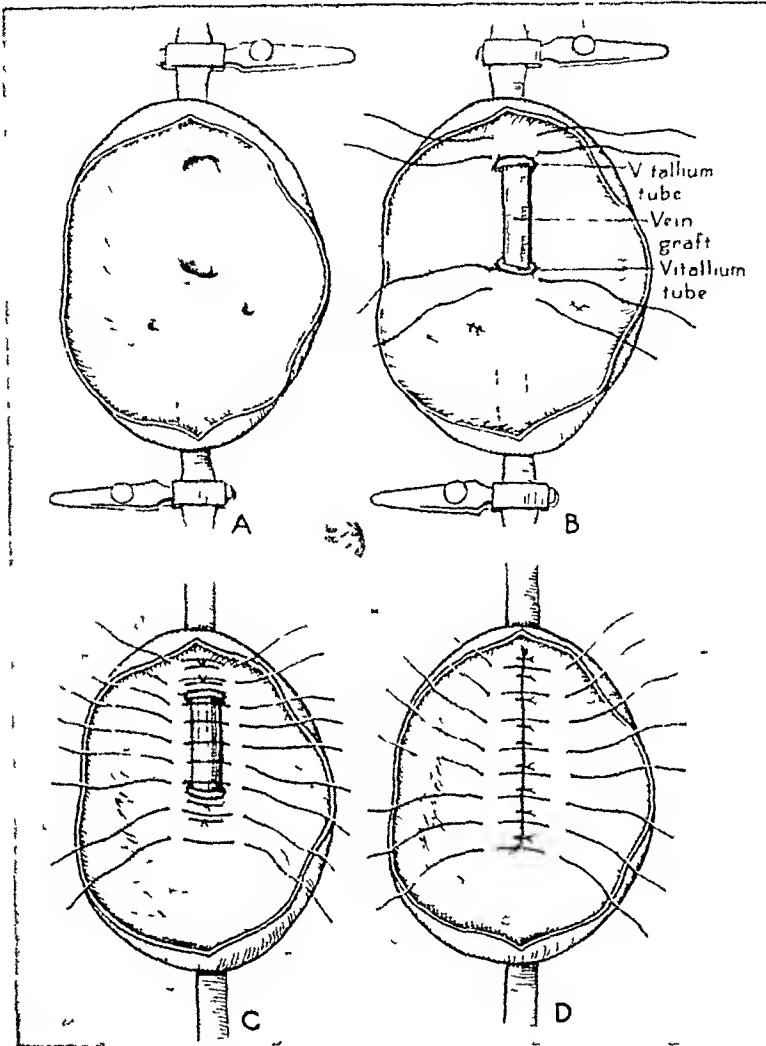


FIG 1—Drawings to illustrate different stages in the nonsuture technique (1) (right) Vitalium tubes employed in the double tube nonsuture technique (2) A vein graft branch ligated flush and clamped distally before being cut (3, 4 and 5) The method of mounting the vein graft upon the tube (6) A vein graft ready for use

## CASE REPORTS

**Case 1**—A 42-year-old colored male entered the Presbyterian Hospital May 27, 1945 complaining of a pulsating swelling in the right thigh of 2½ years duration. His



**FIG 2**—(A) An aneurysm with the sac incised to show the parent artery openings and other branch openings (B) The vein graft with a vitallium tube on either end cannulating the proximal and distal orifices of the parent artery The proximal holding suture ligatures of heavy silk and the distal suture ligatures of finer silk for coapting vein intima to artery intima are shown in place ready to be tied (C) The vein graft with the suture ligatures about the tubes tied Note the rubber shod clamps have been removed permitting the anastomosis to function at this stage Sutures are layed for covering the graft (D) The first row of sutures tied covering the graft with a second row layed

past history was given as follows Pemle lesion in 1923 In 1926 the patient received 100 intravenous and 70 intramuscular injections because of the presence of a positive Wassermann. In 1934 the Wassermann was still positive but became negative following another series of treatments for syphilis over a 3-year period In 1940 the patient received

a bullet wound over the anterior aspect of the right thigh. Two and one-half years later a pulsating swelling developed on the medial aspect of the thigh.

*Examination* Presenting on the medial aspect of the right thigh, lower middle third, was noted a pulsating swelling the size of a large grapefruit. At the same level, over the anterior aspect of the thigh, a round scar one centimeter in diameter was present. Auscultation revealed the presence of a systolic murmur over the tumor. The superficial veins below the knee were engorged. One could not be sure of feeling pulsation over the posterior tibial artery on the right. Pulsation over the dorsalis pedis artery on the right were faint in comparison with the left.



FIG 3—An arteriogram of the femoral artery in Case 1. Note the vitallium tubes with the intervening vein graft. Slight angulation at the proximal end suggests that the vein graft is a little redundant.

On May 31, 1945, the aneurysm was operated upon through an intra-saccular approach. The defect in the femoral artery was bridged with a vein graft bearing a 5 mm vitallium tube on either end. Wound healing following operation was by primary intention. No observer could feel a pulsation over the posterior tibial artery postoperatively. Some thought a faint pulsation was detected on different occasions over the right dorsalis pedis artery but there was no full agreement on this point. However, the oscillometric readings from the lower 1/3 of the right leg were 1/2 division consistently and the patency of the anastomosis was confirmed by arteriogram on the 11th postoperative day.

Figure 3 shows an arteriogram of the femoral artery (Case 1) showing the vein

graft anastomosis and the vitallium tubes in place. The angulation of the vein graft suggests some redundancy.

*Follow-up* The patient was examined on follow up visits 3 mos, 6 mos, 12 and 22 mos postoperatively. The man has had complete exercise tolerance. The reports on being able to palpate a pulsation in the dorsalis pedis artery on the right have varied much as obtained in the early postoperative days previous to arteriographic demonstration of the patency of the anastomosis. The oscillometric readings at 22 mos follow up was  $\frac{1}{2}$  division on lower  $\frac{1}{3}$  of leg—the same as during the early postoperative days.

**Case 2**—A 39-year-old Italian woman who was admitted to the Presbyterian Hospital October 29, 1945, complaining of a pulsating swelling in the left groin of 18 months' duration. This patient had suffered from rheumatic heart disease dating back to an attack of rheumatic fever at age five.

The present illness began in April 1944 with fever, malaise and loss in weight. One day pain in the left groin suddenly appeared, accompanied by a pulsating swelling. The pain gradually subsided over a two-week period. Finally, some months later, the patient was diagnosed as having streptococcus viridans endocarditis with a mycotic aneurysm of the left femoral artery. The infection was cured with penicillin therapy in September 1944, but the aneurysm continued to grow. After the aneurysm had been present one year (some six months before admission) symptoms of intermittent claudication in the left leg appeared.

*Operation* (Nov 23, 1945) Exploration revealed a saccular aneurysm of the common femoral artery with fibrotic occlusion of the distal opening. The latter finding explained the recent history of intermittent claudication and the absence of palpable pulsations over the posterior tibial and dorsalis pedis arteries in this case.

The defect in the femoral artery was bridged with a graft taken from the right superficial femoral vein. The proximal opening of the artery was intubated with a 5 mm vitallium tube bearing the cuffed vein. It was necessary to slit the distal opening 1 cm to get beyond the area of fibrotic occlusion. Even though the femoral artery was badly contracted at this point it was possible to introduce a 4 mm vitallium tube mounted on the other end of the vein graft. When the femoral artery was deoccluded proximally and distally, a substantial pulse was palpable in the artery distal to the anastomosis.

Follow-up oscillometric readings on this patient from the distal  $\frac{1}{3}$  of the leg immediately following operation were up to  $\frac{1}{4}$  division.

On the 13th postoperative day an arteriogram confirmed the patency of the anastomosis.

Oscillometric readings have been maintained at  $\frac{1}{4}$  division from the distal  $\frac{1}{3}$  of the leg in this case now in excess of one year since operation. She is free of symptoms of circulatory insufficiency in the leg.

**Case 3**—A 68-year-old man who was admitted to the Presbyterian Hospital September 5, 1946, because of swelling of the right leg, pain and swelling behind the knee of eight months' duration. For some two years the patient had had transient pains in the calf of the right leg upon exercise. The swelling and pain in the popliteal space had grown progressively worse over the eight months' period prior to admission. For three months prior to admission the leg below the knee had become greatly swollen.

*Examination* The right leg was considerably larger than the left. The surface veins were engorged. Occupying the entire popliteal space was a pulsating mass over which one could hear a systolic murmur. Pulsations in the right dorsalis pedis and posterior tibial arteries were less prominent than on the left. Oscillometric readings from the upper third of the right (affected) leg ( $2\frac{1}{2}$  div) were approximately two thirds of those from the left leg. There was evidence of arteriosclerosis. The Wassermann test was negative.

*Operation* September 12, 1946, revealed an arteriosclerotic fusiform aneurysm of the right popliteal artery which measured 18 centimeters in length. The parent artery above and below the aneurysm was controlled by tapes. The aneurysm sac was opened

clot evacuated and small vessel openings sutured. Finally a femoral vein graft from the left leg mounted on two 8 mm tubes was introduced to bridge the arterial defect within the sac and the sac was closed over the graft.

Following operation the oscillometric readings from the upper 1/3 of the right leg approximated those from the left leg representing an increase of 35 per cent above the preoperative level. Pulsations in the right foot arteries were increased equal to those on the left by palpation.

Follow-up At four and six mos respectively, following operation oscillometric readings from the two legs have remained equal (2½). Pulsation can be palpated throughout the vein graft. The man is active and free of symptoms of circulatory insufficiency in the right leg.

Figure 4 is an x-ray of the leg taken in the lateral position and shows the two vitallium tubes.

**Case 4**—A 50-year-old colored man who was admitted to the Vanderbilt Clinic February 14, 1947, complaining of pain in the chest of four months' duration.

The patient gave a history of lues, insufficiently treated, in 1925. One and one-half years ago (1945) the patient was operated upon for an aneurysm of the right femoral artery. Since operation the patient has had to rest after walking four blocks on account of pain in the calf of the right leg.

Four months prior to admission the patient developed pain in the upper left chest followed by hoarseness two months later. There was a gradual loss of 12 lbs in weight. He developed a non-productive cough and became short of breath on slight exertion.

Examination in the clinic revealed the presence of an aneurysm of the upper descending thoracic aorta. The Kline test was negative.

The patient was placed on bismuth therapy February 18, 1947. Shortly afterward he developed pain in the left popliteal region.

Upon admission to the Presbyterian Hospital on March 6, 1947, the patient was found to have a tender pulsating mass occupying the lower 2/3 of the left popliteal space. A loud systolic bruit was heard over the mass. There was distention of the superficial veins of the left leg below the knee. Pulsations in the left dorsalis pedis and posterior tibial arteries were good. The oscillometric readings from the lower 1/3 of the left leg at a pressure of 80 were two in comparison with ½ for the right leg at the same pressure and level. (The right femoral artery had been operated upon for aneurysm 1½ years before.)

The left leg was placed in extreme elevation. Large doses of codeine were required for the relief of pain. An alcoholic sympathetic ganglia block was done on 1, 2 and 3 left lumbar ganglia. A dry and warmer foot resulted.

On March 13, 1947, the popliteal aneurysm was operated upon. Through an intrasaccular approach a 10-centimeter vein graft, taken from the superficial femoral vein of the same leg was employed to bridge the defect in the lower popliteal artery. A 5 mm vitallium tube was used to mount the vein graft proximally and a 4 mm tube distally. A good pulsation was felt in the left dorsalis pedis artery at the conclusion of the

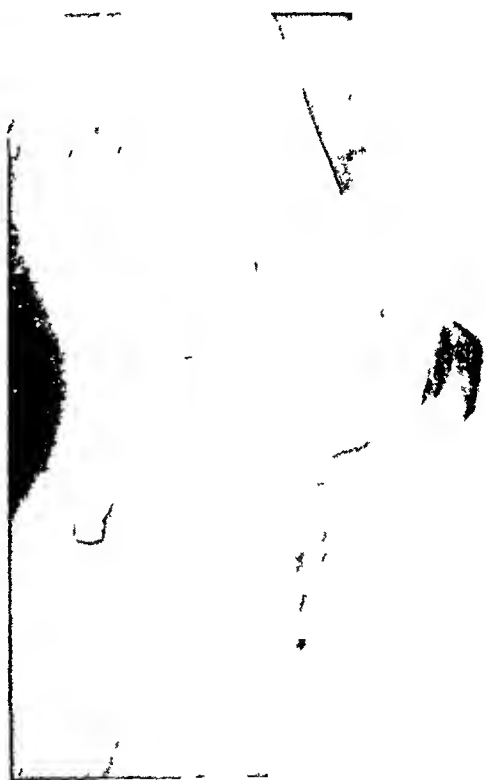


FIG 4—A lateral X-ray of the knee region of the leg in Case 3. Note the vitallium tubes and the presence of calcification in the wall of the artery proximal to the upper tube.

operation On the day following operation the distal pulse remained good and the oscillometric reading from the lower  $\frac{1}{3}$  of the left leg was  $1\frac{1}{4}$  divisions at a pressure of 80 On the third postoperative day the oscillometric readings are two divisions at 80 mm pressure—representing a rise to the preoperative level At 10 days postoperatively the wound is healing by primary intention and the oscillometric readings are being maintained

#### DISCUSSION

There are some points of interest that would seem worth while discussing in connection with these four cases

In Case 1, for example, all observers agreed to the absence of a palpable pulse over the posterior tibial artery following operation but agreed that, on occasion, a faint pulse could be detected over the dorsalis pedis artery During the above convalescent period the presence of oscillometric readings of  $\frac{1}{2}$  division from the distal  $\frac{1}{3}$  of the leg was taken as strong evidence of patency of the anastomosis This evidence was finally confirmed by arteriography

Similarly, Case 2, the patient who for six months had had, upon exercise symptoms of insufficient blood flow due to aneurysm with complete occlusion of the left common femoral artery, likewise had no certain palpable pulsations in the pedal arteries following a restorative operation Again, as in Case 1, the oscillometer afforded dependable evidence (as confirmed by arteriography) of the status of the arterial anastomosis The collateral circulation about the obstructed common femoral artery in this case before operation afforded an oscillometric reading that barely constituted a flicker of the needle After restoration of blood flow by operation, an oscillometric reading of  $\frac{1}{4}$  division from the distal  $\frac{1}{3}$  of the leg has been maintained

It is granted there are factors affecting oscillometric readings such as degree of arteriosclerosis, vasomotor tone blood pressure, etc That must be taken into consideration when comparing readings between different individuals Due to the ages of Cases 1 and 2 it seems unlikely that arteriosclerosis is an important factor In neither Case 1 or 2 had the vasomotor factor been neutralized by sympathetic interruption Case 2 does have the low systolic blood pressure frequently encountered in rheumatic mitral disease

Notwithstanding the above it is not unreasonable that the comparative differences in oscillometric readings between cases 1 and 2 is in the major part accounted for on the basis of the size and location of the arterial anastomoses For example, considering the fact that readings were taken from the distal  $\frac{1}{3}$  of the leg in each case, it is but logical that the distance between the site of the anastomosis and the oscillometer plus the fact that the artery enlarges proximal-ward would, when in addition the size of the anastomosis is considered, greatly affect the magnitude of the oscillations It is not surprising then that an anastomosis of the common femoral artery employing a 4 mm vitallium tube, as in case 2, should yield an oscillometric reading of just half the magnitude of that afforded by a 5 mm tube anastomosis of the superficial femoral at a more distal level, as obtained in case 1 Case 2, it may be recalled, registered an oscillometric reading of  $\frac{1}{4}$  division in comparison with  $\frac{1}{2}$  division in case 1

Of more importance, demonstrating the relatively greater effect the size of the vessel distal to the anastomosis has upon the magnitude of the oscillations, is the greater contrast with Case 4. A defect in the popliteal artery was bridged by a vein graft employing a 4 mm. tube on the distal end. In this case the anastomosis yielded an oscillometric reading of two divisions from the distal  $\frac{1}{3}$  of the leg. Other possible factors affecting the oscillometric readings in Case 4 is (1) the patient's age, (50 years)—some 10 years older than Cases 1 and 2. (2) Interruption of the sympathetic nerves to the extremity.

It is of further interest to state that analysis of the four cases operated upon employing the vein graft inlay technique revealed the salvage of all important collateral vessels.

#### CONCLUSION

The importance of restoring a pulsating arterial blood flow for the complete restitution of function in legs with damaged or diseased primary arteries was long ago emphasized by Matas<sup>1</sup> and Makins.<sup>3</sup> More recent evidence has been brought to bear on the subject by Bigger,<sup>4</sup> Maybury,<sup>5</sup> Freeman,<sup>6</sup> Heringman,<sup>7</sup> and the author.<sup>2</sup>

In the light of the above facts it is to the best interest of the patient to restore a pulsating arterial blood flow if it can be accomplished without damage to important collateral vessels.

Endoaneurysmorrhaphy employing a vein graft inlay restores a pulsating arterial blood flow without damage to important collateral vessels.

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# THE "BORROWING-LENDING" HEMODYNAMIC PHENOMENON (HEMOMETAKINESIA) AND ITS THERAPEUTIC APPLICATION IN PERIPHERAL VASCULAR DISTURBANCES\*

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IT IS NOW A WELL ESTABLISHED FACT that the volume of organs undergoes spontaneous, and even rhythmic, variations, primarily attributable to changes in the volume of the blood within the particular part. When more refined technics of plethysmography were developed, it became practical to carry out accurate quantitative studies of the fluctuations in volume in such peripheral parts as the pinnae, the fingers and the toes, and thus to secure much valuable information under normal resting conditions as well as in diseased states.

There are still numerous gaps in our knowledge of the precise nature of, and the numerous factors involved in, this mechanism, but certain facts have been established which not only have a fundamental physiologic significance but which also appear to have a definite bearing upon certain clinical conditions. It is the purpose of this communication to consider these facts as the basis of a concept which we have chosen to call the "borrowing-lending" phenomenon and for which we are suggesting the term hemometakinesia. We believe that this concept will provide a more rational approach than now exists toward the management of disturbances in the peripheral vascular circulation.

## PLETHYSMOGRAPHY

The plethysmogram, which is the completed record of the plethysmograph, is essentially an ordinary type of Cartesian coordinate, with volume represented on the ordinate and time represented on the abscissa. It is thus a record of the changes in volume, in relation to time, of the particular part enclosed in the extremity cup. These recorded volume changes are the algebraic summation of many volume changes occurring in various degrees and directions in many different portions of the enclosed part<sup>1</sup>. Essentially, however, the changes in volume of the part represent changes in the volume of the vascular bed of the part.

Systematic studies with the plethysmograph have established the fact that small blood vessels in such peripheral parts as the pinnae, the fingers and the toes undergo spontaneous variation in volume. The resting individual, in a comfortable environment, presents at least five types of rhythmic changes in

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volume<sup>1, 2</sup> as follows (1) pulse deflections, (2) respiratory deflections, (3) alpha deflections, (4) beta deflections, and (5) gamma deflections (Figs 1-4) These changes which are conveniently (and arbitrarily) expressed as per 5 cc of part, range in volume from less than 0.1 to 350 or more cu mm

*Pulse Deflections*—Pulse deflections are obviously produced by the heart beat They represent, in the main, the changes in volume of the part brought about by the blood delivered into the part with each heart beat (Fig 1) The volume of the pulse deflections varies considerably, but in the normal resting individual the mean values have been found to be 6.9 cu mm in the tips of the fingers, 4.0 cu mm in the tips of the toes, and 4.1 cu mm in the pinnae<sup>2</sup> The frequency of pulse deflection varies with the heart rate

It is generally accepted that these changes in volume occur primarily within the arteries and arterioles, but it is believed that relatively large volume changes probably occur within the capillaries also, because of their number and total volume It also seems likely that the veins and venules contribute to the pulse volume deflections It is even possible that the volume changes within the arteriovenous anastomoses, capillaries, veins and venules in combination are of greater importance than those within the arteries and arterioles

*Respiratory Deflections*—Respiratory deflections, which represent variations in volume occurring with the normal respiratory cycle, are most highly developed in the pinnae and least well developed in the toes (Fig 1) Their volumes vary from less than 0.1 to 5 cu mm per 5 cc of part<sup>2</sup>

The respiratory deflection depends primarily upon the variations in the venous return to the heart brought about by respiration Parallel with the increase in venous flow produced by inspiration there occurs a relatively rapid emptying of the venous blood from the part and a resultant decrease in its volume With expiration, on the other hand, the relatively rapid rate of venous flow is retarded, and there is a resultant relative increase in the volume of the part

Other factors possibly play a role in this mechanism, but too little is known about them at this time to warrant further comment Of particular interest, however, is the special type of respiratory deflection which occurs in the fingers and toes immediately following a deep inspiration<sup>1, 2</sup> There is first a spontaneous, sudden decrease in the volume of the part, varying from 5 to 105

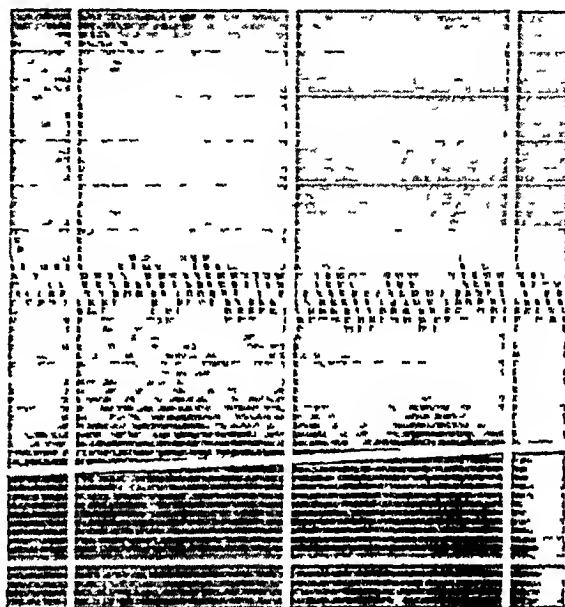


FIG 1—Plethysmogram of normal individual showing pulse deflections (reflecting the heart beats) and respiratory deflections which are represented by variations in the base line Heavy white vertical lines indicate an elapsed time of 15 seconds

cu mm, and more prominent in the fingers than in the toes. At the same time the pulse deflections also show a decrease in volume. Shortly after these phenomena are observed, vasodilatation begins and continues until the previous pulsatile characteristics are resumed. Before vasodilatation is complete, however, a series of small alpha waves appear, varying from 2 to 8 cu mm. After two or more successive deep inspirations, the extent of the response is progressively diminished until eventually a sort of tachyphylaxis occurs and vasoconstriction ceases to appear. The volume change is lessened as the interval between inspirations is shortened. The volume change is not necessarily concordant, it may show either an increase or a decrease. Interestingly enough, it is not as definite, as predictable or as large in the pinnae as in the fingers and toes.

*Alpha Deflections*—Alpha deflections, which occur less frequently than respiratory deflections, are usually smooth in contour, but are not uniform (Fig. 2). They vary in frequency and size, with a tendency toward an inverse relationship. The mean frequency has been found to be 7.9 per minute in the finger tips, 7.7 in the toes, and 8.6 in the pinnae,<sup>2</sup> and the mean volume for these respective parts has been found to be 14.5, 7.1 and 6.6 cu mm.<sup>2</sup> Alpha deflections seem to vary from person to person, and even in the same person variations in the different peripheral parts are not necessarily concordant. Although they are independent of variations in arterial pressure,<sup>3</sup> these deflections are predominantly under the control of the sympathetic nervous system, they almost entirely disappear following interruption of sympathetic pathways.<sup>2</sup>

The volume changes represented by alpha deflections are due essentially to variations in volume of the blood within the part, but their frequency suggests the possibility that variations in lymph volume may be a contributing factor. The studies of Webb and Nicoll<sup>4</sup> on the bat's wing showed that contractions of the lymphatics are responsible for much of the flow of lymph, and McMaster's studies<sup>5, 6</sup> on other animals support these observations. Whether or not similar contractions occur in man is not known, but the frequency and rate of the lymphatic contractions observed in animals are of such a character as to permit them to be responsible for some part of the alpha deflections.

Alpha deflections indicate gross or total changes in the vascular bed slower than those produced by the pulse and respiratory deflections. Only a limited portion, and not necessarily all, of the vascular bed may undergo such volume changes at one time. Although the function of these shifts of blood volume is not now known, some significance seems apparent.<sup>2</sup>

*Beta Deflections*—Beta deflections are larger waves upon which is superimposed the succession of smaller alpha deflections (Fig. 3). They vary in frequency from one-half to two per minute and their volume range is from 5 to 60 cu mm.<sup>2</sup> They have been observed in all parts studied. Their frequency and volume are totally irregular, but they tend to vary concordantly in the fingers, toes and pinnae. Beta deflections are also considered to represent primarily volume changes in the vascular bed but as is also true of alpha

FIG 2

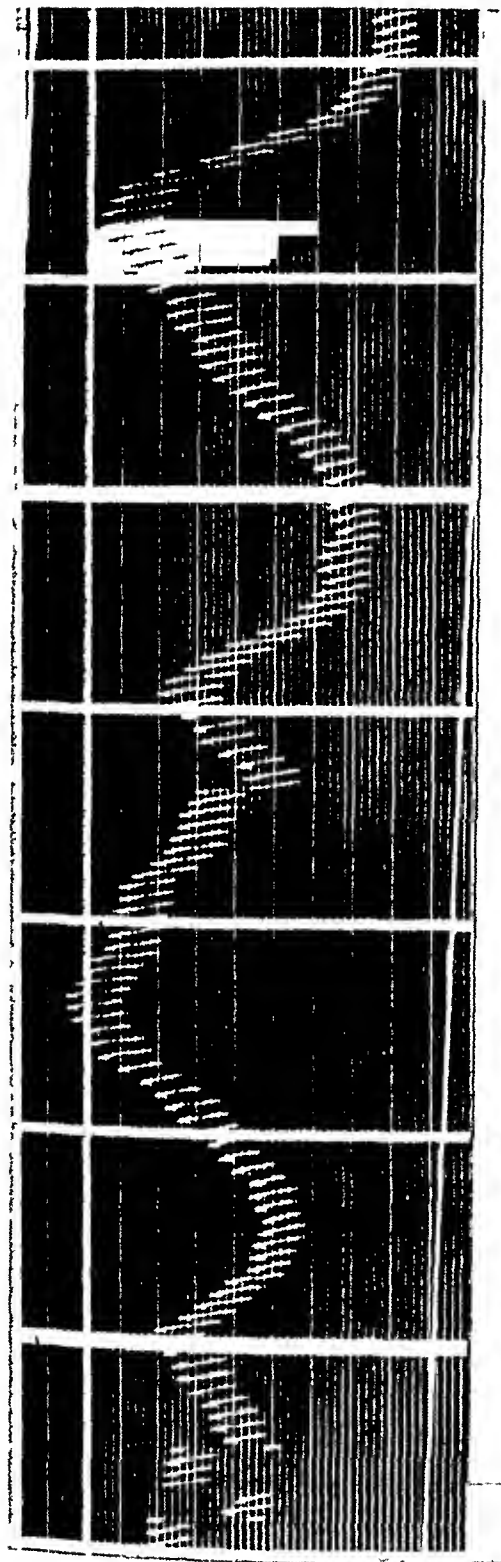


FIG 3

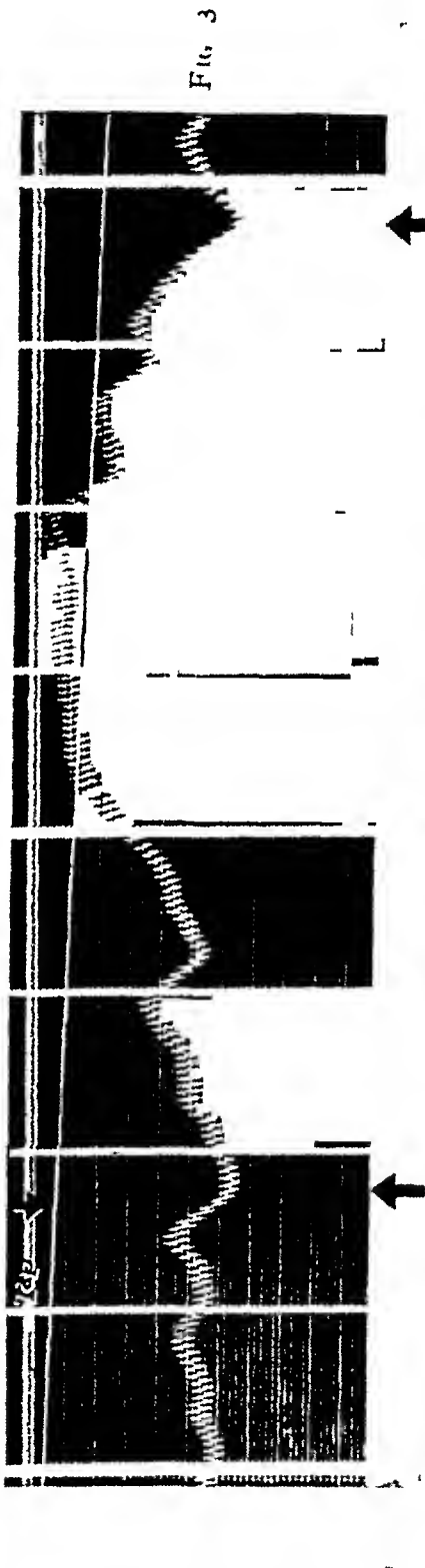


FIG 4

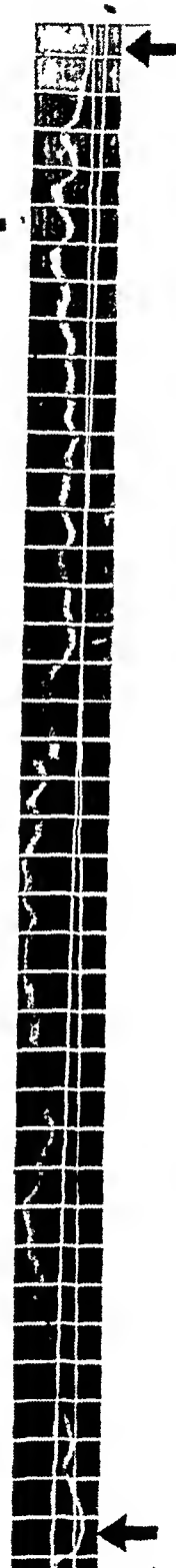


FIG 2—Plethysmogram of normal individual showing alpha deflections represented by the marked variations in the base line

FIG 3—Plethysmogram of normal individual showing a positive and a negative beta deflection extending between the arrows Alpha deflections are superimposed upon the beta deflections

FIG 4—Plethysmogram of normal individual showing a positive and negative gamma deflection extending between arrows Alpha and beta deflections are superimposed upon the gamma deflections

deflections, a significant part of these changes may be due to variations in lymph volume. It is possible, in addition, that changes in intercellular and intracellular volume contribute to them.

*Gamma Deflections*—Gamma deflections (Fig. 4) develop more slowly than any of the other deflections. They are probably concerned with large, and usually with relatively slow, shifts in blood volume from one part of the body to another. They range in frequency from one to eight per hour and in volume from 50 to 350 cu. mm.<sup>2</sup> Although the relationship is not necessarily constant, they show a tendency to vary concordantly in the fingers, toes and pinnae. Like the other deflections, the gamma waves are predominantly the result of changes in volume of the vascular bed of the part, with variations in lymph volume probably contributing significantly to the volume change.

#### NORMAL VARIATIONS IN THE PLETHYSMOGRAM

The plethysmograms of normal individuals under certain circumstances present variations of considerable degree which may resemble the changes found in diseased states. For this reason it is desirable to review them briefly. Of particular importance among the factors which may produce such changes are (1) the psychic state of the individual, (2) the environmental temperature, (3) the relation of the part to the heart level, and (4) interruption of the sympathetic pathways to the part.

*Psychic State*—Both the pulse and the alpha deflections may be greatly influenced by the psychic state. Fear, anxiety, or tenseness on the part of the subject, even as a reaction to the study, tend to produce a diminution in the pulse and alpha deflections and an increase in the rate of pulse deflections,<sup>7, 8</sup> apparently as the result of an increased sympathetic activity associated with the psychic disturbance which causes an increase in vasomotor tone. Any change in the mental state may affect the character of the spontaneous volume deflections. Flushing or blushing, for instance, is associated with an increase in the volume of the pulse deflections and a decrease in the alpha deflections, while if the individual is comfortable and relaxed, the volume of the pulse deflections is moderate and that of the alpha deflections is relatively large.

*Environmental Temperature*—The spontaneous volume deflections are considerably influenced by the environmental temperature. Chilling the subject, either by local applications or in a cool room, produces vasoconstriction and a consequent reduction in the volume of the pulse and alpha deflections. In general, the degree of vasoconstriction is proportionate to the degree of chilling. After prolonged chilling, vasodilatation may supervene, the result being an increase in the volume of the deflections, in which the alpha deflections usually exhibit a relatively greater change than the pulse deflections. With prolonged chilling, however, a negative gamma deflection also occurs, indicating a slow but definite over-all decrease in the volume of the part. As the part warms, a positive gamma deflection appears, indicating restoration of local blood volume and an over-all increase in the volume of the part.

The application of heat either locally or in a heated room, has the reverse

effect, that is, vasodilatation occurs, with a consequent increase in the volume of the pulse deflections and a decrease in the alpha deflections, while a positive gamma deflection appears, indicating an over-all increase in the volume of the part

It has been suggested<sup>1</sup> that these reactions serve as good tests for organic occlusive arterial and arteriolar disease. In such conditions as thrombo-angitis obliterans and obliterating arteriosclerotic endarteritis the vasodilating responses are impaired or absent. The effort to produce vasodilatation in the finger tips or the tips of the toes by the application of heat to another extremity tests the patency of the arteries and peripheral blood vessels to the part under investigation, as well as its neurovascular mechanism.

*Relation of Part to Heart Level*—Spontaneous volume deflections are influenced by the position of the part in relation to the heart level. A decrease in volume of the pulse and alpha deflections may be produced by placing the part below heart level, the decrease being generally proportionate to the degree of lowering of the part. The pooling of blood and lymph in the dependent part, as a result of gravity, produces a positive gamma deflection.

The exact explanation of the decrease in volume of the pulse deflection has not been definitely established, but two factors, either alone or in combination, may account for it. The first is arteriolar constriction. The second, and more likely, is distention of the vessels, with a diminution in further distensibility of the vessel walls.<sup>9</sup>

Elevation of the part above heart level produces results just the opposite of those produced by dependency, that is, there is a pronounced increase in the volume of the pulse deflections, and, as a consequence of the draining out of the blood within the part, a negative gamma deflection. Obviously, for standard recordings, the part should be kept at or near heart level.

*Interruption of Sympathetic Pathways*—The interruption of impulses over the sympathetic pathways produces profound changes in the spontaneous volume deflections. Within a few minutes after the regional sympathetic nerves or ganglia have been blocked by infiltration with 1 per cent procaine hydrochloride solution there is a marked increase in the volume of the pulse deflections and a virtual disappearance of the alpha deflections. The latter phenomenon would be expected, since these deflections are dependent upon intact sympathetic pathways.

It has been our observation that sympathetic block produces a maximum degree of vasodilatation in the part, which cannot be exceeded, and which is seldom equaled, by any other clinical procedure. During the early phases of sympathetic block the resulting engorgement of the vascular bed within the part produces a positive gamma inscription.

Sympathetic block furnishes another significant diagnostic test<sup>10, 11</sup>. By this means it is easy to determine the degree of the normal, or, in certain conditions, of the abnormal, vasoconstrictor tone and the extent of vasodilatation, or the general order of the amount of increase in vascularity of the part which can be achieved by interruption of the sympathetic pathways.

THE "BORROWING-LENDING" HEMODYNAMIC PHENOMENON  
(HEMOMETAKINESIA)

From what has been said, it is evident that spontaneous variations are constantly taking place in the vascular bed in different parts of the body, with resulting changes in the distribution of the blood volume. These changes may occur in widely separated parts of the body. They may be rhythmic, concordant, or discordant. They may be produced by intrinsic factors not yet well understood, or they may be influenced by various internal and external stimuli. Fundamentally, they indicate a continuous shifting back and forth of blood from one part of the body to another.<sup>12</sup>

It has been repeatedly demonstrated that there are spontaneous variations in the volume of certain internal organs, as well as in the volume of superficial structures. Experimental studies in animals have demonstrated intermittency or irregularity in the blood flow of the renal glomeruli,<sup>13</sup> tongue and skeletal muscles,<sup>14</sup> and ear.<sup>15</sup> Further experimental studies on the circulation in various organs by Zweifach<sup>16</sup> and Chambers and Zweifach<sup>17</sup> have confirmed the intermittency of blood flow in various parts of the body, a phenomenon which these workers term vasomotion. The spontaneous variations in splenic volume reported by several observers<sup>18-22</sup> are of a magnitude and frequency comparable to those of the beta and gamma deflections observed in plethysmographic studies of human subjects.

The alpha, beta and gamma deflections observed on plethysmograms clearly indicate that spontaneous shifts in the blood flow are constantly taking place within the vascular system. There is evidently a continuous "borrowing and lending" of blood (hemometakinesia) to meet variations in local requirements.

The volume of the vascular system is quite variable within certain limits. In the average normal individual (a 70-kg man) the system is filled with approximately 5,400 cc of blood<sup>23</sup> at a pressure which varies from 120 to 80 mm of mercury, with a mean pressure of about 93 mm. Great variations can take place in the vascular bed within a relatively short period of time, especially in isolated parts of the body, but the total blood volume, under ordinary conditions, remains relatively constant.

The vascular volume of a finger or toe can be observed to double in size within a matter of minutes. The filling of this augmented vascular bed with blood, however, obviously does not imply the doubling of the total blood volume of the body, nor is there reason to believe that there exists in the body a special reservoir of blood for such purposes. Yet the blood must come from some source. The obvious explanation is that it has come from the vascular bed of other parts of the body. It is achieved without any alteration at all in the total blood volume, by adjustment of the vascular bed (Fig 5). An increase in the volume of the vascular bed in one part of the body and a decrease by the same amount in another part increases the volume of blood in the former at the expense of the latter without any variation in the total blood volume (Fig 5).

With disease, local needs may increase and may remain elevated for long periods of time. Should an infection develop in a finger, for instance, blood is

shifted into the finger at the expense of other parts of the body with less urgent demands, and inflammatory hyperemia results. The shift is probably brought about by the local release, as a consequence of infection, of substances which produce arteriolar, capillary and venous dilatation. In other words, the "stop-cocks" are opened locally in the finger and more blood is borrowed temporarily from other parts of the body to aid in overcoming infection.

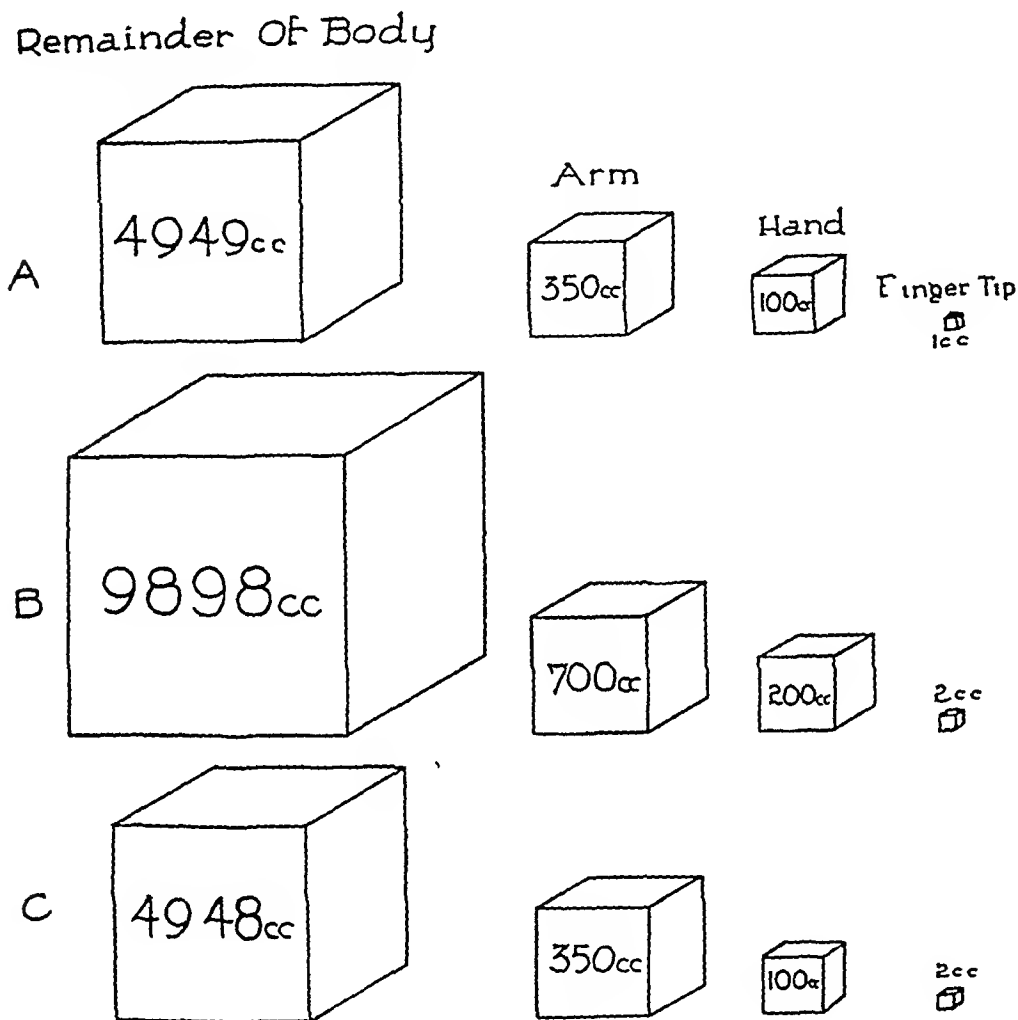


FIG 5—Schematic representation of the "borrowing-lending" hemodynamic phenomenon (hemometaknesia). Cubes are drawn to scale to represent volume of vascular bed in different parts of the body. A Normal vascular bed, assuming a total blood volume of 5,400 cc. B Vascular volume when component parts are all doubled. C Vascular volume when blood volume of only one part, the finger tip, is doubled, with this increment of blood being derived or "lent" from the "remainder of body." It is apparent, when B and C are compared to A, the normal, that the same purpose is achieved in C as in B, the doubling of the blood volume of the finger tip, with no variation in the normal relationship in C but with obvious disturbance of it in B.

The amount of blood borrowed in this hypothetical case is relatively small, perhaps 1 cc, but it is sufficient to double, approximately, the normal local blood volume. An increase of this extent, however, in the blood supply of the finger does not disturb the general blood volume nor its hemodynamics. No effort is made by the body to double its general vascular volume in order to



double the volume in the finger. The body mechanisms do not produce for this purpose a generalized vasodilatation. This would not only be unnecessary. It would actually defeat the purpose. Were the vascular bed suddenly to double in volume, a great disproportion would develop, with equal suddenness, between the volume of the bed and the available supply of blood, and the subject as a result, would collapse (Fig 5).

With the total blood volume relatively fixed, it would be impossible to increase the circulating blood volume in any single part or tissue if there were a comparable increase in the volume of the entire vascular system. Furthermore, if the volume of the entire vascular bed were suddenly to double, and if the volume in one part, such as the hand, trebled, the drop in the intravascular pressure or blood pressure would be so great that the blood flow in the hand would be impaired rather than improved.

On the other hand, in the absence of generalized vasodilatation, even with maximum local vasodilatation the pressure head in the arterial system can be maintained, thus permitting in the local part an increase in volume of blood flow per unit of time. A response such as this is inevitable in order to obey fundamental principles of hemodynamics and at the same time to maintain normal circulation.

These spontaneous variations in blood volume in different parts of the body quite evidently are not mere chance occurrences. They seem, instead, to be part of a well regulated mechanism, with definite order and significance, concerned with certain vital functions such as proper thermal regulation, nutrition, repair, hemodynamics and other physiologic adjustments.

It is conceivable that at least a part of this significance lies in the attempt by the body to utilize its total blood volume in the most efficient possible manner. Obviously, the total blood volume in the body at any one time is too small to meet the maximum demand of all the tissues at the same time should a disease state arise to precipitate such a situation. On the other hand, it is more than sufficient to meet urgent local demands for large quantities of blood in isolated parts such as a finger, hand, foot, or even an entire extremity.

#### SPECIAL STUDIES

Numerous observations made upon normal individuals as well as on patients with various forms of peripheral vascular disease have invariably been consistent, regardless of the methods employed to determine and record variation in blood flow. Special studies have been made by thermometric and plethysographic methods.

These studies are done routinely, under controlled atmospheric conditions, in a room constructed to reduce psychic disturbances. Following rest in bed for a sufficient period of time to permit stabilization of the vascular system plethysmograms are obtained for the distal phalanges of the fingers and toes (usually the index finger and the second toe) as well as of the pinnae. Thermograms are obtained for these parts as well as for other areas, a total of 20 areas, distributed bilaterally and symmetrically, is usually observed. Plethys-

mographic and thermometric observations are usually made simultaneously. The response to such measures as interruption of sympathetic innervation, reactive hyperemia, drugs, environmental and local temperature changes, and psychic and neurogenic factors are observed as reflections in the plethysmograms and thermograms.

Observations made upon two patients, selected from the large number upon whom these studies were made, are presented to illustrate the "borrowing-lending" phenomenon (hemometakinesia).

**First Patient**—G. Y., a white male 45 years of age, suffered with mild intermittent claudication due to early senile arteriosclerosis. Plethysmographic and thermometric studies were made after the patient had rested in bed in the observation room (room temperature 78° F, relative humidity 70 per cent) for 60 minutes. The skin temperature determinations were made bilaterally for the third toe, the dorsum of the foot, the mid pretibial area, the knee, the mid thigh, and the chest. The plethysmographic determinations were made for the distal phalanges of the right index finger and for the second toe on each side. After a state of stabilization had been reached, a left lumbar sympathetic block (first through fourth ganglia) was performed with 1 per cent procaine hydrochloride solution.

Within a few minutes after the performance of left lumbar sympathetic block the following events occurred simultaneously (Fig. 6).

- 1 A rapid elevation of the skin temperature of the left leg, with marked flushing
- 2 A significant increase in the volume of pulse deflections of the left second toe
- 3 An increase in the total volume of the tip of the left second toe
- 4 A fall in the skin temperature of the right leg and the chest
- 5 A decrease in the volume of the pulse deflections of the right second toe and right index finger
- 6 A decrease in the total volume of the tip of the right second toe

These changes indicated a marked vasodilatation in the left lower extremity after sympathetic block, with a considerable increase in the volume of blood and rate of blood flow. Blood was "borrowed" by the left leg at the expense of the remainder of the body. It was "lent" by the right leg and right index finger, as indicated by the cooling of the skin and the decrease in volume of pulse deflections and the total volume of these parts.

The expense of the shift, however, was not borne entirely by the right leg and right hand, since the vascular changes indicating a decrease in blood volume and blood flow were not as great as those reflecting the increase in the left leg. This might be expected. When relatively large quantities of blood are shifted to a part as large as the lower extremity, no single part of the body would be expected to suffer the entire loss, even if it were capable of "lending" it all. An index finger obviously would not be able to meet the whole demand, even if all its blood were shifted to the leg. Furthermore, if all the blood of a part such as the finger were shifted to the area of special need, the lending part would suffer serious damage from ischemia. Normal physiologic adjustments provide a mechanism whereby no organ is made to give up or "lend" its blood to an extent which would produce serious injury. Depending upon the quality and quantity of the shift, every organ that can afford to "lend" blood elsewhere does so. Under ordinary circumstances, however, each organ gives up only a small fraction of blood, and the changes reflecting a decrease in blood supply are relatively small in any one part under observation.

**Second Patient**—J. H., a Negro male 34 years of age, who was suffering with a marked anxiety neurosis, was subjected to the same tests as the first patient and was also studied by certain additional procedures. A venipuncture was performed initially, with much deliberate manipulation, in order to produce pain and anxiety and to induce psychic

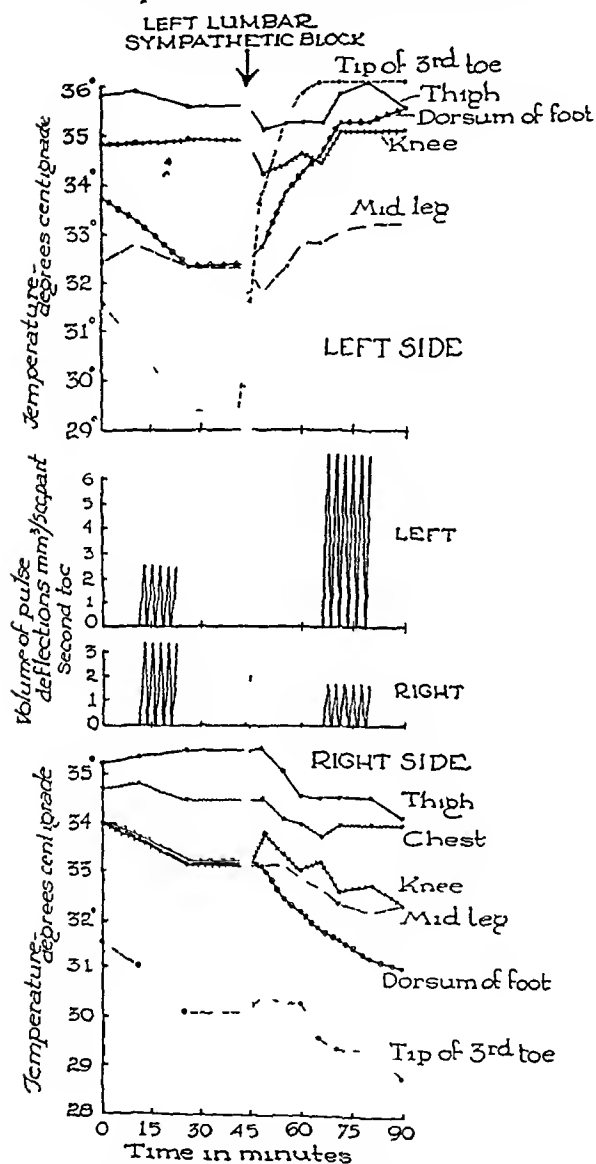
Surface Temperature and Pulse Volume  
Response to Sympathetic Block

FIG 6—Surface temperature and pulse volume responses to left lumbar sympathetic block. It is obvious from the chart that following the block there was vasodilatation with increased blood flow in the left lower extremity, indicating the "borrowing," while on the right side there is evidence of diminished blood flow, indicating "lending" of blood

tension and consequent diffuse vasoconstriction. After the vascular state had been stabilized at the level of vasoconstriction, 5 cc (500 mg) of tetraethylammonium chloride was injected intravenously. Then, after sufficient time had elapsed for the reaction to subside, a left posterior tibial nerve block was performed, using 1 per cent procaine hydrochloride solution. Two and a half hours later, a left lumbar sympathetic nerve block (first through fourth ganglia) was performed, using the same drug.

## Studies In Peripheral Vascular Responses

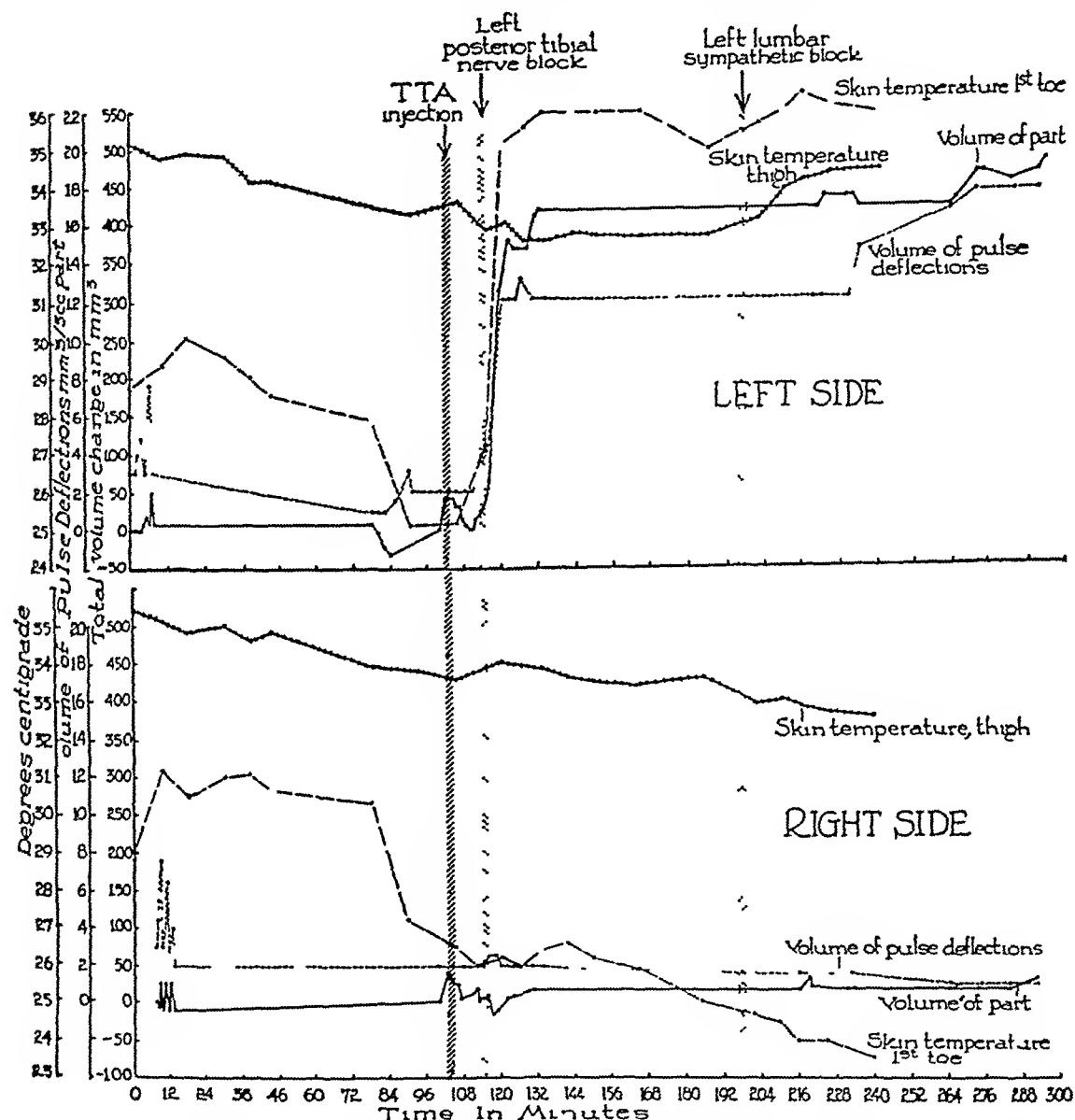


FIG 7—Graph showing thermometric and plethysmographic changes following injection of tetraethylammonium chloride (T T A), left posterior tibial block and left lumbar sympathetic block

The phenomena observed in the first patient are still further clarified by the results obtained in the second patient (Fig 7)

The anxiety following the traumatic venipuncture resulted in considerable decreases in skin temperature, in the volume of pulse deflections, and in the total volume of the tips of the finger and toes studied. All these findings are evidence of diffuse vasoconstriction.

After the administration of tetraethylammonium chloride, which has been reported to produce vasodilatation,<sup>24</sup> there was little or no change in the skin temperature or in the

volume of the tips of the second toes, and only a slight increase in the volume of the pulse deflections of the finger and toes studied. Very little vasodilatation was to be expected. With generalized vasodilatation, each organ must "lend" and "borrow" at the same time, which is impossible unless the blood volume or cardiac output or both are increased to meet the demands occasioned by diffuse dilatation. Any drug which is a strong vasodilator would be expected at least to restore the state of the blood vessels of the superficial portions of the body to resting normal levels, which tetraethylammonium chloride did not do in this case. Furthermore, there is no evidence to show, nor any reason to expect, the sympathetolytic effects to be greatest where the sympathetic tone is greatest. If the drug acts equally throughout the sympathetic ganglia, diffuse vasodilatation would be expected to result in little change in the blood supply to a particular part unless blood volume or cardiac output or both were increased.

Following left posterior nerve block the following changes were observed (Fig. 7)

- 1 An increase in the skin temperature of the left first toe
- 2 An increase in the volume of pulse deflections of the second toe
- 3 An increase in the total volume of the tip of the left second toe

There were no changes on the right. The changes on the left, it should be noted, occurred in spite of the patient's state of anxiety and after the administration of tetraethylammonium bromide had failed to produce vasodilatation. Since the amount of blood that would be borrowed by a part as small as a foot to meet even maximum vasodilatation is relatively small, no measurable evidence of "lending" would be expected to be observed in other portions of the body, especially since each part might participate in supplying only a very small amount of blood.

At the end of two and a half hours there was relatively little change in the state of the circulation under observation. When left lumbar sympathetic block was done at this time, the following changes occurred:

- 1 A further increase in the temperature of the skin of the left leg and thigh
- 2 A further increase in the volume of pulse deflections of the left second toe
- 3 A further increase in the total volume of the tip of the left second toe
- 4 A slight decrease in the volume of pulse deflections of the right second toe
- 5 A slight but definite decrease in the temperature of the areas with intact sympathetic innervation

After left lumbar sympathetic block, the volume of blood shifted to the whole left leg was evidently much greater than that following tibial nerve block, and, as in the first patient, evidence of a shift of blood from the right leg and right hand were obtained (Figs. 6 and 7).

#### DISCUSSION

The evidence now at hand seems to justify the following statements:

- 1 There is a continuous shifting back and forth of blood from one part of the body to another
- 2 The "borrowing" and "lending" of blood (*hemometaknesia*) from tissue to tissue to meet variations in local requirements seem indicative of a well regulated mechanism which permits the body to utilize its limited total blood volume in the most efficient manner
- 3 The essence of this mechanism seems to lie in the control and regulation of the vascular bed, which permits an increase in the volume of blood of one part of the body with a corresponding simultaneous decrease in the volume of blood in other parts
- 4 The variation of the blood volume in different parts of the body does not involve any alteration in the total blood volume

5 Variations in cardiac output, however, can produce changes in blood flow to a part independent of changes in blood volume

The application of these principles of hemodynamics to peripheral vascular disease immediately suggests itself. Peripheral vascular disease is characterized by a disturbance of, or actual diminution in, the normal amount of circulating blood which reaches the part, and its effective therapy is based on improvement in the circulation or an increase in the blood supply of the part. Therapeutic measures designed to produce dilatation of the entire vascular bed do not seem rational for a disease state localized to a single peripheral part, but in spite of the illogic of the attempt, there are numerous reports concerning the production of generalized vasodilatation as a form of therapy for peripheral vascular disease involving portions of the body. The results of these efforts are open to question, theoretically such measures are inefficient. Moreover, even if an effective agent, *i e*, with the ability to produce *maximum* vasodilatation, for this purpose did exist, its effects would be dangerous, the reaction would be shock-like, and the original purpose of increasing the blood supply to the local part would be completely defeated.

In view of the lack of rationale in peripheral vascular disease of the use of agents intended to produce generalized vasodilatation, quite aside from their ineffectiveness and theoretical dangers, the attention should be concentrated on measures which produce local vasodilatation. The best of these measures, in our experience is sympathetic denervation of the affected part. It is rational, because it conforms with the principles of hemodynamics just laid down, it produces local vasodilatation insuring maximum improvement in the local circulation of the diseased part. It is safe, because it does not reduce the arterial blood pressure or produce serious systemic disturbances by the sudden creation of a disproportion between the total volume of the vascular bed and the total blood volume. Finally, it is effective. Theoretically, when this procedure is used, there should be a definite and significant increase in blood supply to the diseased part. Practically, there is such an increase, as is demonstrated by the two cases presented in this communication, which were selected from a large experience.

Indeed, we have yet to find a general vasodilator which could produce in a local part, such as the toes, fingers, foot, hand, or extremity, vasodilatation equal in degree or duration to that produced by sympathetic denervation of the part.

#### SUMMARY

1 Although gaps still exist in our knowledge of the hemodynamics of the peripheral circulation under normal resting conditions and in disease states, the evidence at hand justifies certain statements

A That there is a continuous shifting back and forth of blood from one part of the body to another; for this "borrowing-lending" mechanism the term *hemometakmesia* is proposed. B That hemometakinesia seems to indicate the existence of a well regulated mechanism which permits the body to utilize its limited total blood volume in the most efficient manner to meet variations in

local requirements C That the essence of this mechanism seems to lie in the control and regulation of the vascular bed, which permits an increase in the volume of blood of one part of the body with a corresponding simultaneous decrease in the volume of blood in another part without any alteration in the total blood volume

2 It is suggested that these principles of hemodynamics are applicable to the management of peripheral vascular disease, the effective therapy of which is based on improvement in the circulation or an increase in the blood supply of the part Measures directed toward the improvement of the local circulation by production of dilatation of the entire vascular bed are of doubtful value, whereas measures directed toward local vasodilatation are in conformity with the natural "borrowing-lending" mechanism (hemometakinesia)

3 The most effective method of increasing the local blood supply is sympathetic denervation of the affected part In addition, it is in complete conformity with the concept of hemometakinesia

4 Two cases, selected from a large experience, are presented to illustrate the concept of hemometakinesia and to demonstrate the value of sympathetic denervation as a therapeutic measure in peripheral vascular disease

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## ARTERIAL INJURIES\*

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WOUNDS OF MAJOR ARTERIES in World War II proved unexpectedly serious as regards survival of the affected limb. The experience of the past seemed to indicate that ligation of torn vessels in the course of debridement was in most instances the practicable method of handling these cases although suture repair and tube anastomoses had been reported. The large number of amputations for ischemic extremities brought about efforts to suture arteries and to bridge gaps by tubes, or venous grafts after the method of Blakemore and Lord<sup>1</sup>. While the value of these methods from the reports so far available, as well as from the series to be presented, cannot be proved statistically, the outcome in individual cases is sufficiently encouraging to warrant further trial in civilian practice.

The basis for this study consists of 114 wounds of major arteries seen in an Evacuation Hospital in the European Theater of Operations together with four primary cases operated on in a General Hospital in the same theater. For purposes of comparison with other reports the Evacuation Hospital cases are tabulated separately. The General Hospital cases were not battle casualties. They are presented after the others and included with them in the discussion.

### MORTALITY

Patients succumbing before, during or immediately after operation have been omitted since the purpose of the study is the incidence of gangrene and measures to lessen it. There were four such fatalities from hemorrhage and shock during the evacuation hospital period. These included one wound of the iliac, two of the femoral and one of the popliteal.

Among the cases included in the series there were four deaths. Two of these had come to amputation for gas gangrene, one died with anuria, and the fourth, a civilian woman, died suddenly the day after operation. She had an amputation of the leg in addition to a wound of the brachial artery which was progressing quite satisfactorily. In general, if a patient with a major vascular wound reaches a hospital his chances of life, if not of limb, are pretty good.

Results of injuries to the major vessels of the extremities appear in Table I.

An attempt was made to keep patients with extremities of doubtful viability until the issue was clear. It was at times impossible, however, so that there may be some error in estimates although it is thought to be small. Necrosis of fingers or toes sufficed to record the outcome as gangrene.

Reports from other Evacuation Hospitals<sup>2, 3, 4</sup> in the ETO substantiate the serious outlook for major arterial wounds as indicated in Table I. On

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\* Read before the American Surgical Association, March 25, 26 and 27, Hot Springs, Virginia

## ARTERIAL INJURIES

the other hand the much more favorable experience which some of the World War I figures show are due to inclusion of cases of arteriovenous and traumatic aneurysms picked up in rear echelons Few of these in my experience were apparent at the evacuation hospital stage

TABLE I  
EVACUATION HOSPITAL CASES

Vessel	Number of Cases	Gangrene	% Gangrene
Axillary	5	2	40
Brachial	51	18	35
Femoral	25	20	80
Popliteal	21	15	71
Post tibial* (upper end)	7	4	57
Ant and post tibials	5	2	40
Total	114	61	54%

\* Wounds of the posterior tibial in the lower part of the leg are not of themselves particularly dangerous and are not tabulated

### TREATMENT

It is obvious that a lateral tear only of the artery represents the condition most favorable for suture When a segment of the vessel is carried away so that a graft or tube is necessary to bridge the gap the outlook is much worse Last but not least the extent of damage to the surrounding tissues in which collateral circulation can carry on has probably been the most important factor in the loss of many limbs

Table II summarizes the experience of attempts at arterial repair in the Evacuation Hospital series

TABLE II  
ARTERIAL REPAIR EVACUATION HOSPITAL CASES

Vessel	Suture	Gang	Suture	Gang	Tube	Gang	Vein	Gang	Total	Gang	%
			Anast		Anast		Graft				Gang
Brachial	2	0	1	0			1	1	4	1	25
Femoral	2*	1	1	1	1 <sup>b</sup>	1	1	1	5	4	80
Popliteal	1	0			2	1			3	1	33
Post tibial	1	0			1	1			2	1	50
									14	7	50

\* Both sutures of incision after removal thrombus

<sup>b</sup> Attempted after two days

### SUMMARY OF EVACUATION HOSPITAL CASES

*Brachial Artery* (4 cases) —The brachial artery of an American soldier was torn half way across in the upper third The extremity was warm but pulseless Following suture of the vessel there was a good recovery

An American soldier received multiple wounds, in one of which the lower brachial was divided except for a thin bridge of intima remaining posteriorly There was no pulse and no oscillometric reading in the extremity although it was fairly warm The vessel was sutured about 15 hours after injury A day after operation the radial pulse and small swings of the oscillometric needle were noted

A German civilian woman suffered multiple mine wounds including division of the brachial in the lower third. The vessel was sutured 24 hours after injury. The next day the pulse was faintly perceptible and on oscillometric examination there were flickers of the needle. The patient died suddenly, 36 hours after injury. Postmortem examination of the anastomosis showed a soft non-adherent clot extending one centimeter upward and two down.

An American soldier received a severe wound of the arm, dividing the brachial artery and the median nerve in the upper third and fracturing the humerus. The extremity was cold and pulseless. Six hours after injury the gap in the artery was bridged by a vein graft using vitallium cuffs. The hand never became warm, nor was any pulse perceptible. At the time of evacuation six days after operation the fingers and thumb were black.

*Femoral Artery* (5 cases) The femoral artery of an American soldier was divided in Hunter's Canal. The foot was cold. The gap between the vessel ends was bridged by a vein graft with vitallium cuffs. No distal pulse was obtained subsequently. At transfer on the 12th day it appeared that at least part of the foot would be lost.

A German boy of eight was brought in with a wound in which the distal end of the femoral artery had been divided. End-to-end suture was done. It appeared that he would eventually come to amputation when he was evacuated on the 5th day.

An American soldier was admitted with an extensive wound of the upper thigh in which the superficial femoral artery was found to be thrombosed shortly below the profunda branch. As the foot was warm it was hoped that the circulation would remain adequate. In the course of the next 48 hours the foot became cold and an attempt was made to save the situation by a tube anastomosis. In view of the time elapsed this was ill-advised. There was no benefit and amputation became necessary.

Two American soldiers with thrombosis of the superficial femoral were treated by incision of the artery, removal of the thrombus and suture. In one of these men a faint pulse was felt distally 45 minutes after operation and thereafter could be obtained on careful examination. The other man had in addition to his femoral thrombosis a fracture of the femur. When discharged on the 7th day he had gangrene of the first and second toes.

*Popliteal Artery* (3 cases) An American soldier was admitted with a gaping wound of the popliteal space. The femur was fractured and the artery divided with ends far apart. The opposite femur also was fractured. The gap in the popliteal artery was bridged by a plastic tube 24 hours after injury. The veins of the foot were observed to fill and color appeared in the skin. Twenty hours after operation the foot was warm but eight hours later had become cold again and went on to gangrene. The patient died on the 5th day with a progressive oliguria. At autopsy the tube contained a soft clot which extended 4 to 5 cm into the artery above and below.

An American soldier suffered division of the popliteal artery by a small shell fragment which did little other damage. The foot was cool rather than cold, pulseless, and the leg without oscillometric response. Eleven hours after injury a plastic tube anastomosis was done. The pulse could be felt immediately after operation and good oscillometric swings obtained. These continued until the 7th day when, without change in warmth of the foot, the distal pulse could no longer be felt nor could an oscillometric reading be made. On the 13th day the pulse could again be faintly felt. The next day the tube was removed. It was filled with clot. The dorsalis pedis continued to be faintly palpable and the patient was evacuated with an intact extremity.

An American soldier's popliteal artery was torn about three-fourths through its circumference in the lower part of its course. The laceration was sutured. Postoperatively

there was some pain and swelling in the leg but when the patient was evacuated on the 6th day he could move the toes, and the foot was warm

*Posterior Tibial Artery* (2 cases) An American soldier had his posterior tibial artery divided above the peroneal branch and both bones of the leg fractured by shell fire. The extremity was cold. A plastic tube anastomosis was done with no immediate nor late improvement and amputation had to be carried out four days later.

A German girl of 16 was brought in with a shell wound of the leg which fractured both bones, divided the anterior tibial artery and made a lateral wound in the posterior tibial in the lower third of the leg. The pulses were absent in the foot which was dusky and cool. At operation 10 hours after injury the posterior tibial was sutured. Recovery was slow but by the 5th day the foot was warm and the circulation was thought to be adequate.

In Table III the result of arterial repair as compared with ligation and series as a whole is presented together with like data from other Evacuation Hospitals.

TABLE III

	Suture		Non-Suture Anast		Combined			Ligation			Whole Series		
	No	Gang	No	Gang	No	Gang	%	No	Gang	%	No	Gang	%
This study	8 <sup>a</sup>	2	6	5	14	7	50	58 <sup>b</sup>	32	55	114 <sup>c</sup>	61	54
Rose, Hess & Welch	5	0	8	6	13	6	46	70	37	53	91 <sup>d</sup>	45	49
Bradford & Moore	6 <sup>e</sup>	1	5	3	11	4	36	87	39	45	110	46	42
Stewart	0	0	5 <sup>f</sup>	2	5	2	40	33	17	52	38	19	50
Totals	19	3	24	16	43	19	44	248	125	50	353	171	48

<sup>a</sup> Includes two cases thrombectomy.

<sup>b</sup> A number of cases are omitted because the record does not specify as to ligation.

<sup>c</sup> The discrepancy between the sum of those treated by operation and by ligation, 72, and the whole series 114 is made up of those in whom nothing was done to the vessel and in whom the records are not sufficiently clear to classify, although it is probable that most of this group were ligated.

<sup>d</sup> Cases of primary amputation omitted.

<sup>e</sup> Includes one case thrombectomy.

<sup>f</sup> Dr Stewart reported two additional cases in which non-suture anastomosis was attempted but they are omitted from the table because they occurred at a period previous to that from which the rest of his series was compiled.

In Table IV figures from the much larger series of Odom<sup>5</sup> and DeBakey and Simeone<sup>6</sup> are presented for comparison with these of Table III. Doctor Odom was surgical consultant to one of the European Armies while the figures of Doctors DeBakey and Simeone were compiled from the records available in the Surgeon General's Office.

TABLE IV

	Suture		Non-Suture Anast		Combined			Ligation			Whole Series		
	No	Gang	No	Gang	No	Gang	%	No	Gang	%	No	Gang	%
Odom	42	23	28	14	70	37	53	767	386	50	857	423	51
DeBakey & Simeone	81	29	54	30	135	59	44	1639	802	49	2471	995	40

## SUMMARY OF GENERAL HOSPITAL CASES

A German prisoner was wounded by a small fragment of cartridge which exploded in a bonfire. It divided the brachial artery 1 to 2 cm above its bifurcation in the forearm. The radial pulse was absent and the extremity cooler than its fellow. The artery was sutured. Immediately after operation the pulse could not be felt but on examining him seven hours later it was just palpable. It became strong before transfer.

A German prisoner slipped, thrusting his elbow through a pane of glass. The brachial artery and median nerve were divided below the middle of the arm. At operation three hours after injury the ends of the artery could be approximated with slight tension and were sutured together. The lower end of the median nerve was not found at this time. Immediately after the operation a radial pulse could not be felt but within an hour it was faintly palpable. On the 16th postoperative day the median nerve was sutured. At this operation although pulsation was present just below, it could not be felt at the site of anastomosis.

A Polish soldier was accidentally shot through the lower thigh with a pistol. The lower end of the femoral artery was divided except for shreds and the vein torn. An end-to-end anastomosis of the artery was made with some difficulty as the knee had to be flexed to approximate the torn ends. The vein was ligated and the leg put up in plaster to maintain flexion. The foot warmed up within a few hours after operation but distal pulses had not been felt at the time he left the hospital one month later.

The popliteal artery of an American soldier was completely torn through opposite the joint in a truck accident, apparently as the result of hyperextension of the knee. There was considerable hemorrhage into the popliteal space. The vein and nerve were intact. As approximation of the torn ends was impossible, a plastic tube anastomosis was done. The lower end of the vessel was found with difficulty and would only take a small tube. No immediate effect was noticeable but 12 hours later the foot, which had been cold, was warm. It soon became cold again and amputation through the thigh was eventually necessary.

## DISCUSSION

*Suture* Including both Evacuation and General Hospital cases, but excluding the two in which suture was of the thrombectomy incision, there were nine arterial sutures with one subsequent gangrene. This would seem to indicate that suture is quite successful as compared with other methods. It must be remembered, however, that it is possible only in lateral wounds or those with limited separation of the divided ends, and therefore, in general, in the less severe injuries. Furthermore the majority of sutures here reported were done in wounds of the brachial artery, in which the outlook for survival of the arm was favorable.

That clotting is likely to take place at the suture site raises the question as to whether the extra time consumed as compared with simple ligation is justified. The ideal, of course, is that the channel remain open, but there is reason to hope that even though clotting occurs, enough blood will get through to maintain viability until the collateral circulation can take over.

The Medical Research Council (British)<sup>†</sup> states "As a general rule it takes four days in the arm and 14 days or more in the leg for the distal pulse to return after ligation of the main artery." Individual cases vary. Rose, Hess and Welch have noted palpable radial pulsations 24 to 72 hours after ligation.

of the brachial artery In a patient in this series whose brachial had to be ligated at the lower end radial pulsations were questionable at the end of 48 hours and present in 72 hours

In two patients with sutured brachials a radial pulse was noted after 24 hours In one of the general hospital cases with a suture anastomosis at the lower end of the brachial the pulse was felt seven hours after operation It had not been examined in the interval since leaving the operating room

As a result of this experience the next patient was observed more closely After suture of his brachial in the lower half of the arm the radial pulse could not be felt in the operating room but within an hour after return to the ward it was just palpable It seems probable that blood carried through the site of anastomosis contributed to this finding

*Plastic tube anastomosis* There were five cases with gangrene in four One of the plastic tube anastomoses of the popliteal in this series resulted most satisfactorily, postoperative observations seeming to indicate that blood was carried through it for six days, at which time collateral circulation was adequate This patient's wound, however, was relatively small, and the foot never more than cool so it may well have been that his collateral circulation was sufficient from the beginning In two other tube anastomoses of the popliteal there was encouragement from the warming of the foot only to see it become cold again after 24 hours and go on to gangrene

*Venous graft* There were two cases with gangrene in both It is more difficult technically than tube anastomosis and failure in these cases may have been due to lack of experience with the method

*Heparin* In debrided battle wounds the employment of heparin parenterally involves a risk In the arterial injuries of civilian life, however, it is to be hoped that it may be employed, as experience both experimental and clinical has shown its value It was used locally in some instances in this series but was unavailable in amount sufficient for systemic heparinization

*Thrombosis* If a vessel is contused by a missile, thrombosis may result DeBakey and Simeone reported 70 per cent amputation following 44 cases of thrombosis In this series there were ten cases recorded of whom four developed gangrene In two of these, both of the femoral in its midposition, the artery was incised, the clot removed and the vascular wound sutured One kept a viable foot and the other developed gangrene of the first and second toes

*Sympathetic Block* Sympathetic block was tried in a large number of the cases in this series with disappointing results The disappointment probably is to be attributed to the hope that it would benefit cadaver-like limbs in which not only the main blood channel but much of the collateral circulatory bed was damaged It seems reasonable to expect that in cases where the margin between a sufficient and an insufficient blood supply is narrow, it may serve to turn the scale

*Ligation of accompanying vein* This subject is raised as the question has excited so much interest In this series there is insufficient data to draw any conclusion

## SUMMARY

Battle wounds involving the femoral and popliteal arteries have resulted in subsequent gangrene in a large proportion of cases. Those of the brachial were followed by loss of the extremity in over a quarter.

Suture of lateral wounds of the arteries should ordinarily be done, and end-to-end sutures in cases where it is practicable.

The use of glass and plastic tubes, or venous grafts to bridge gaps does not seem, from the statistics available, to have improved results, yet a consideration of individual cases justifies further trial.

In the surgery of civilian vascular injuries, particularly those in which large debrided areas do not have to be left open, heparin offers an opportunity of bettering the outcome.

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# SYMPATHECTOMY FOR OBLITERATIVE ARTERIAL DISEASE; INDICATIONS AND CONTRAINDICATIONS\*

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THE PURPOSE OF SYMPATHECTOMY in the treatment of peripheral vascular disease is manifestly to abolish the vasomotor tone in order to improve the circulation and to allow development of collateral blood vessels. The greater the impairment of circulation by vasoconstriction, the better are the results to be expected from sympathetic denervation. In those cases, however, in which vasomotor tone is low, sympathectomy may be of little value. In addition, widespread sympathectomy, may actually produce harm by lowering the peripheral resistance, especially in cases where there is severe arterial obliteration. This paper presents an evaluation of sympathectomy in the treatment of obliterative arterial disease, and a discussion of the indications and contraindications for the use of this form of treatment.

The peripheral circulation serves a dual function. By means of blood flow through the capillaries the nutrient demands of the tissues are met. In addition, the peripheral circulation to the extremities in man serves the purpose of regulating the body temperature. In accordance with the requirements for conservation or dispersal of heat, the circulation to the extremities is reduced or expanded. This dual function of the circulation is mediated by a dual control. With vasomotor nerves intact, the circulation through the distal parts of the extremities can be shown to be influenced reflexly through stimulation or inhibition of the sympathetic nerves. After removal of this vasomotor control by sympathectomy the circulation is dependent upon the metabolic requirements of the tissues.<sup>1</sup>

In view of this dual function and dual control, the presence of a dual anatomic structure is to be expected. That such is the case was shown originally by the researches of Sucquet<sup>2</sup> and Hoyer.<sup>3</sup> They first described the neuromyo-arterial glomus, a vascular arrangement quite distinct from the nutrient capillaries, which, in man, was found chiefly in the distal parts of the extremities. The studies of E. R. Clark<sup>4</sup> on the rabbit ear provided knowledge of the structure and activities of these arteriovenous anastomoses in the experimental animal. Understanding of the physiology of these structures was made possible through the investigations of Grant<sup>5</sup> and Bland.<sup>6</sup> By means of these communications between the terminal arteries and the small veins of the extremities, blood can rapidly be shunted from the arterial to the venous system.

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without passing through the capillary network Grant<sup>5</sup> showed that these communications were under vasomotor control since stimulation of the sympathetic nerves caused them to close, as did the injection of adrenalin Clark<sup>4</sup> observed that injury to the nerve caused the arterio-venous anastomosis to remain continuously dilated for 10 to 14 days After that time, the smooth muscle apparently acquired tonicity and the lumen thereafter was maintained at a narrow calibre This observation may help to explain the evanescence of cutaneous vasodilatation after nerve injury, although it fails to account for the persistent

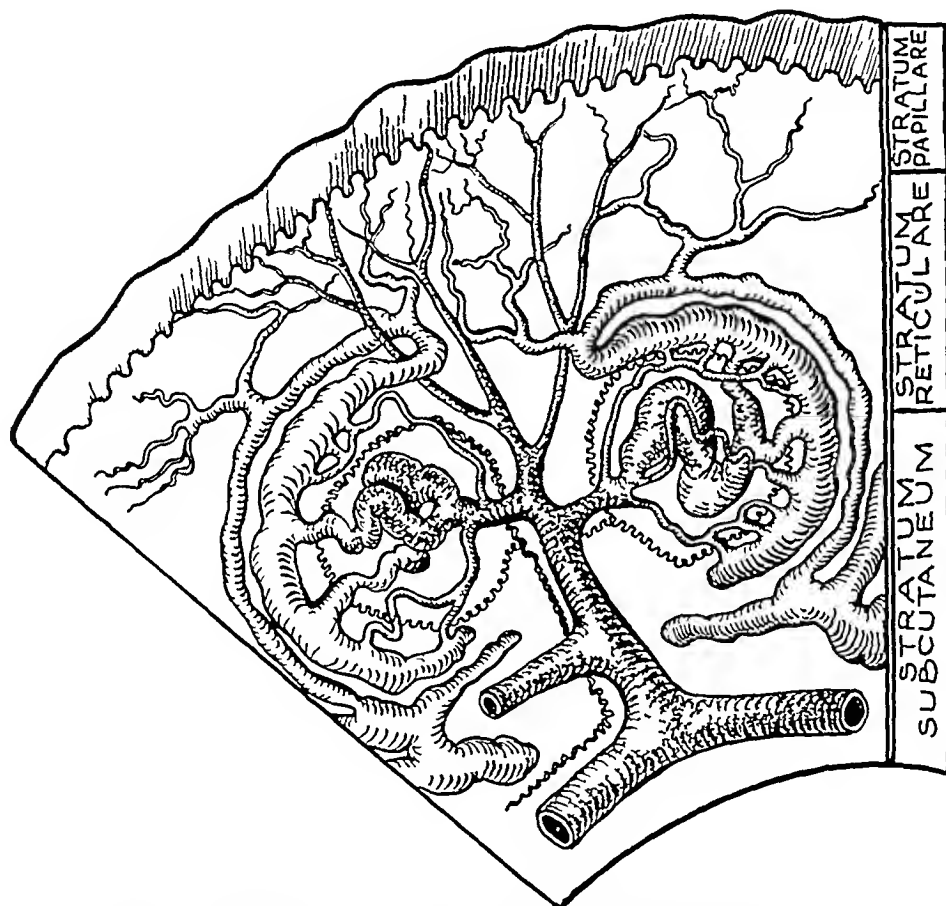


FIG 1—Anatomic arrangement of arteriovenous anastomoses as found in the ventral surface of the digit (Redrawn after Popoff Arch Path 1934)

and prolonged vasodilatation, especially in the lower extremities, which follows sympathectomy From observations on experimental animals and man, it seems likely that the increased peripheral skin temperature which follows interruption of sympathetic impulses is mainly due to opening up of these arterio-venous communications

Popoff<sup>7</sup> called attention to the significance of these arterio-venous anastomoses in peripheral vascular diseases after careful anatomic studies with reconstruction from serial sections The anatomic arrangements are shown in Figure

1, which has been redrawn from Popoff's paper. He stressed the fact that when arterial blood passes directly into the veins without going through the capillary network, serious deprivation of the tissues may result. In addition, in thrombo-angitis obliterans he described abnormal arterio-venous communications which might lead to a rapid dumping of the arterial blood into the veins. Figure 2 represents a schematic drawing of the A-V anastomoses taken from Popoff's original work. Microscopic changes in the veins led him to conclude that "Arterialization of the veins is evidently the result of adaptation of the veins to abnormal strain created by an uncontrollable flow of blood through the artero-venous anastomosis." In one patient he even went so far as to compare the oxygen saturation of blood obtained from a vein on the dorsum of the

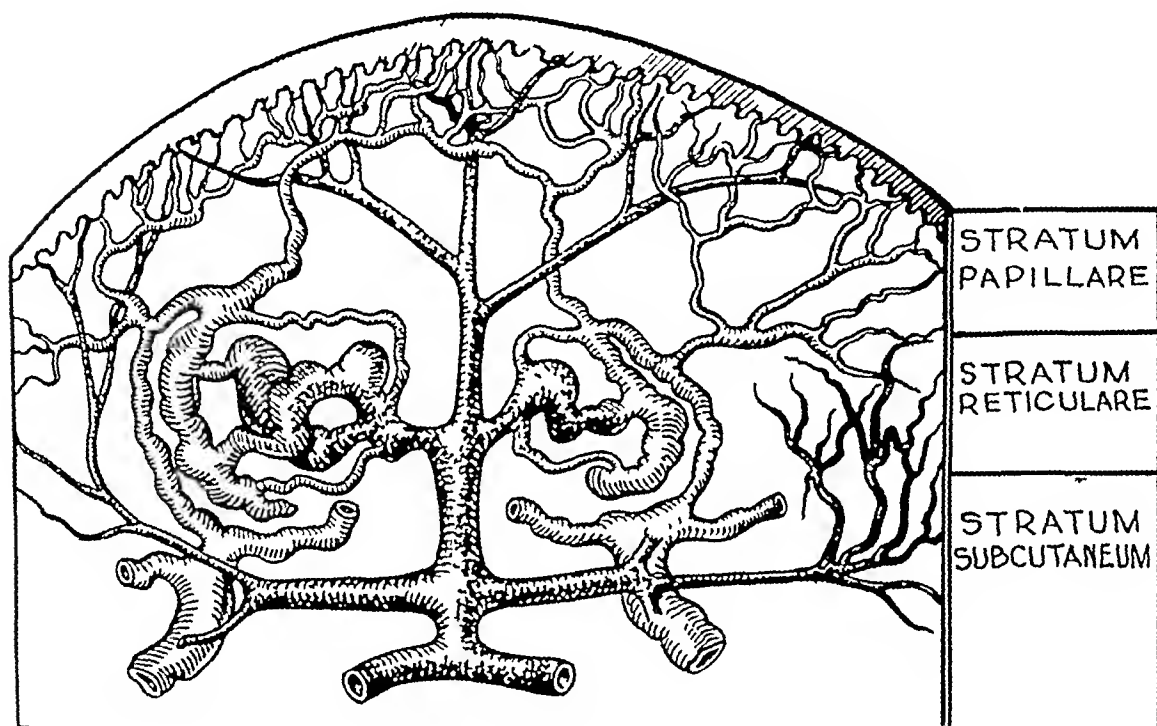


FIG 2—Diagram demonstrating two types of anomalous arteriovenous anastomoses found in thromboangitis obliterans: the lateral type and the terminal type of anastomoses (Redrawn after Popoff Arch Path 1934)

foot with that of blood simultaneously obtained from a forearm vein. As he expected in view of his anatomic studies, he found that the oxygen saturation of the blood from the veins of the foot was considerably higher than that of the blood obtained from the arm, suggesting that the blood in its passage from the arteries to the veins had not traversed the capillary loop. This observation was confirmed and extended by Harpuder, Stein, and Byer,<sup>8</sup> in a series of cases. Some of the highest oxygen values which they found were in cases in which the disease was the most advanced. They concluded that "shunt circulation, for practical purposes, is a loss as far as tissue metabolism is concerned." To Atlas<sup>9</sup> goes the credit for having suggested that the disastrous results occasionally encountered after sympathectomy in advanced arterial obliterative

disease were due to opening up of these small arterio-venous communications

The chief indication for sympathectomy is abnormal vasoconstriction or vasospasm. In extreme cases such as the digital syncope of Raynaud's phenomenon, the diagnosis of this condition is simple, but it is far more difficult to arrive at a sound basis for making this diagnosis in the less severe cases.

Brown<sup>10</sup> was the first to approach the problem of placing vasomotor tone in man on a quantitative basis. He compared the rise in skin temperature of the digits with the rise in mouth temperature after the administration of typhoid vaccine. The change in the surface temperature of the digits gave an index of vasodilatation. Morton and Scott<sup>11</sup> used anesthesia, general, spinal or local, to abolish vasomotor tone. They designated the average maximum vasodilator response of undiseased arteries as "the normal vasodilatation level." White<sup>12</sup> was the first to use paravertebral injection of procaine to block the sympathetic nerves to the extremities as a test to evaluate the potential benefit of sympathetic ganglionectomy. The vasodilatation with rise in skin temperature which occurs upon heating the unaffected extremities or portions of the body was employed by Gibbon and Landis<sup>13</sup> to differentiate vasospastic from occlusive arterial disease. All of these vasodilatation tests are useful in estimating the degree of organic vascular occlusion, but they do not indicate the relative degree of vasoconstriction which is intermittently or constantly affecting the blood supply to the peripheral tissues. Vasoconstriction is the normal physiologic response of the body to cooling. It occurs both in normal patients and in those with diseased or injured blood vessels. The vasodilatation tests indicate only to what extent the peripheral blood vessels can dilate, they do not measure the degree of vasoconstriction.

In order to make the diagnosis of abnormal vasoconstriction, certain clinical signs have been utilized. In the selection of patients with intermittent claudication for sympathectomy, the combination of peripheral cyanosis, increased sweating, and constriction of superficial veins of the extremities was used by Freeman and Montgomery<sup>14</sup> as clinical evidence of high vasomotor tone. Experience with sympathectomy in obliterative arterial disease during the past five years leads us to re-emphasize the significance of these clinical signs of abnormal vasoconstriction. Possibly less attention is paid now than formerly to the prominence of the veins on the dorsum of the foot, since we have repeatedly observed patients whose veins were prominent, but in whom other signs indicated a high degree of vasomotor tone. Constricted veins, however, are still looked upon as good evidence of abnormal vasoconstriction. One further observation which is probably of significance is delayed blanching of the extremity on elevation. This delay in the drainage of blood from the foot may well be due to venous constriction and probably indicates concomitant arterial constriction, which sympathectomy is designed to relieve.

The vasodilatation test, as commonly performed, may not allow sufficient time for the blood vessels to dilate to their maximum capacity. This fact is suggested by the frequency with which it is noted that the rise in surface temperature following lumbar ganglionectomy exceeds the highest level obtained

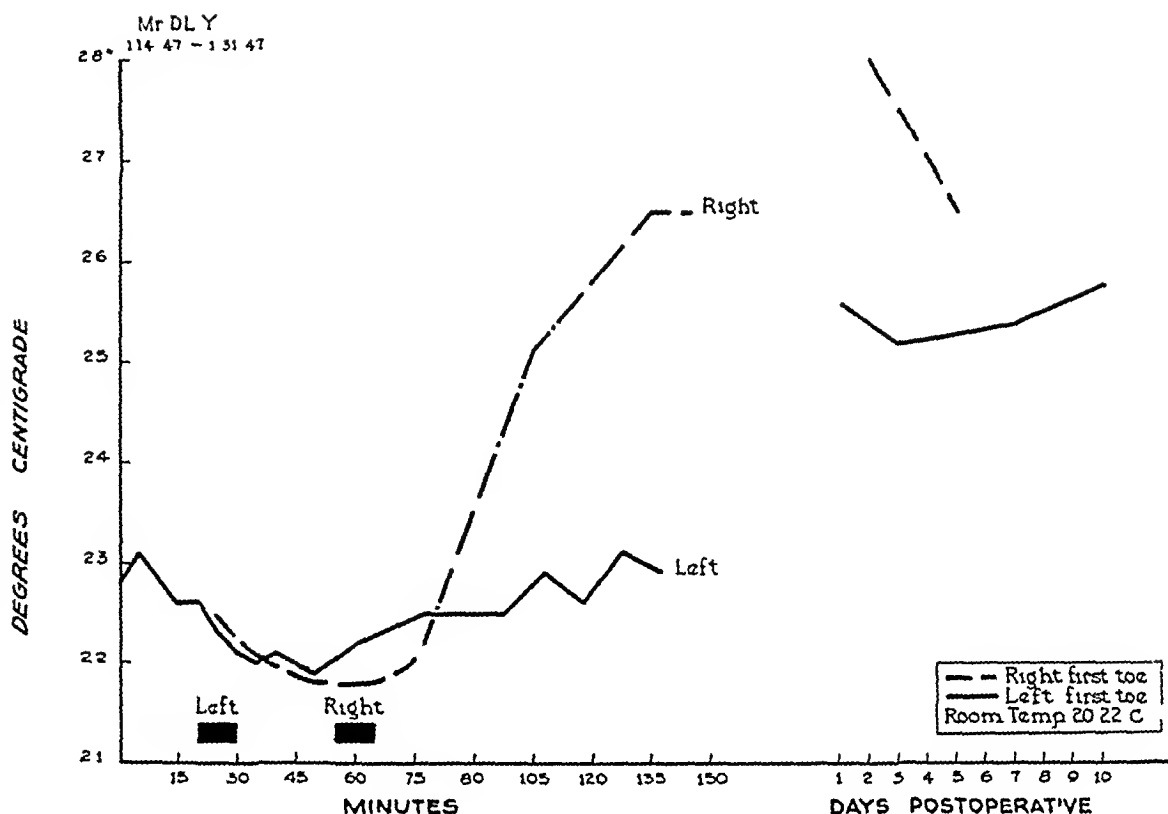


FIG 3—Skin temperature increase following lumbar sympathetic blocks and lumbar sympathectomies in a patient with thromboangitis obliterans

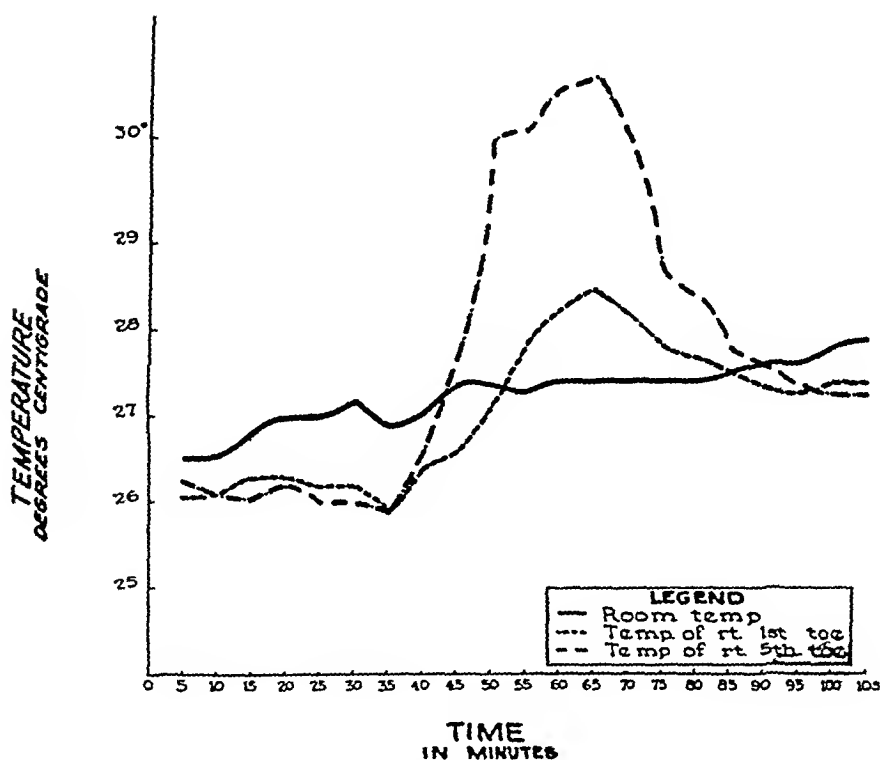


FIG 4—Skin temperature changes following right lumbar sympathetic block in patient with erythrocyanosis frigida

during the vasodilatation test. Figure 3 shows the skin temperature increase following lumbar blocks in a patient with severe thromboangitis obliterans. It can be seen that in the days following lumbar sympathectomies, the surface temperatures consistently exceeded those observed at the height of the vasodilatation tests. Subsequent studies on this patient have confirmed the value of the operations. We have come to place great reliance upon the subjective improvement, noted by the patient after temporary removal of vasomotor control by blocking the sympathetic ganglia with procaine, as an indication for sympathectomy. The indications for sympathectomy and the results obtained in a small group of patients with obliterative arterial disease are shown in Table I.

Failure of the skin temperature to increase to normal levels through vasodilatation after release of vasomotor tone does not necessarily indicate that the vasomotor tone is low. The arterial obstruction may be of such severity that it is impossible, even with the opening up of collateral channels, to deliver sufficient blood flow to the distal parts of the extremity to raise the surface temperature to normal levels. On the other hand, vasoconstriction may further reduce the circulation to the tissues. Previously, many patients were excluded from the benefits of sympathectomy, because of the failure of the surface temperature to reach normal high levels following temporary interruption of vasomotor control. In the case illustrated in Figure 4, the patient had suffered from erythrocyanosis frigida of both lower and upper extremities for many years. She developed a painful ulceration beneath the nail of her right great toe, which failed to heal in four months. Immersion of the forearms in hot water (Landis-Gibbon test) failed to produce any rise in the temperature of the toes. Blocking of the posterior tibial nerve with 2 per cent procaine resulted in a rise in skin temperature of only 2 degrees centigrade. With lumbar sympathetic block, as shown in Figure 4, the skin temperature increase was more pronounced and there was great improvement in the color of the extremity, as well as relief from pain. Bilateral lumbar sympathectomy subsequently performed, resulted in complete relief of her symptoms.

The quantity of blood which can be delivered to the peripheral tissues in a given period of time depends not only upon the diameter of the arteries supplying the part, but also upon the peripheral resistance. Lowering of the peripheral resistance in any section of the vascular bed proximal to the nutrient capillaries, especially those in the distal portions of the extremities, necessarily reduces the effective pressure. The effect upon the height of oscillations measured at the ankle of lowering the peripheral resistance by opening up of blood vessels in the working calf muscles has been previously reported. This resistance was shown to be a significant factor in the distribution of blood to the peripheral tissues. It was suggested at that time that extensive sympathectomy might be contraindicated in the presence of advanced obliterative arterial disease, since the peripheral resistance might be so lowered in the proximal portion of the limb as to curtail the flow of blood in the more distal parts of the extremity. Atlas<sup>9</sup> has shown that in three patients lumbar sympathectomy allowed a rise in the surface temperature of 2 to 5 degrees centigrade above

TABLE I  
INDICATIONS AND RESULTS OF SYMPATHECTOMY IN OBLITERATIVE ARTERIAL DISEASE

Case No	Patient	Age	Diagnosis	Condition of Extremity	Lowest Palpable Artery	Indications for Sympathectomy	Operation	Results	Late Improvement
1	P A Male U C H 124118	48	T A O 10 mos	1 Spontaneous amputation of distal phalanx of 6 fingers and sclerodactylia of all fingers 2 Tips of fingers show painful ulcers 3 Numbness and tingling of toes	1 Arteriogram shows radial blocked and blocks of digital arteries 2 Ankle pulses present bilaterally.	1 Cold, clammy extremities 2 Improvement in arteriogram after lumbar sympathectomy block	1 Bilateral upper thoracic sympathectomy 2 Bilateral lumbar sympathectomy (L-1, 2, 3, 4)	1 Stumps of fingers healed completely 2 Pain, numbness and tingling of feet have ceased	++
2	O L Y Male U C H 136430	49	T A O 7 wks	1 Cold, aching feet bilaterally 2 Weakness and dragging left foot 3 Intermittent claudication, lf foot, 1 block 4 Spotty ischemic neuritis	1 Lf popliteal 2 Rt dorsalis pedis (rt post tibial absent) 3 Rt ulnar obliterated	1 Cold, clammy extremities 2 Moderate venous constriction 3 No improvement in claudication with lumbar sympathectomy block, but color improved	1 Bilateral lumbar sympathectomy (L-4 only)	1 Coldness and aching pain gone 2 Improvement in strength, lf foot 3 Claudication time improved x 20 4 Spotty ischemic neuritis decreased greatly and finally disappeared	+++
3	O M Female U C H 131147	47	Raynaud's with considerable local arterial obliteration 10 yrs	1 Erythrocyanosis frigida, upper and lower extremities 2 Extreme cyanosis rt large toe with ulceration	1 Ankle pulses present bilaterally	1 Cold, clammy cyanotic extremities 2 Venous constriction with delayed blanching time 3 Improvement with lumbar sympathectomy block (good color, warmth and relief of pain)	1 Bilateral lumbar sympathectomy (L-2, 3, 4)	1 Improvement in color warmth and pain 2 Ulcer healed	+++
4	W S Male Franklin 2321	52	Arteriosclerosis obliterans 9 mos	1 No excoriation some rubor 2 Colder rt extremity 3 Numbness of toes 3, 4, 5 on rt 4 Intermittent claudication, rt, 1 block	1 Rt femoral 2 Lf posterior tibial	1 Cold clammy rt foot 2 Delayed blanching time 3 Claudication improved after lumbar sympathectomy block on 2 occasions	Rt lumbar sympathectomy (L-1, 2, 3)	1 Rt foot warmer 2 Claudication time improved x 4 3 Numbness in toes disappeared	++
5	F Z Female Franklin 1998	41	T A O 15 yrs.	1 Lf foot colder than rt 2 No ulcers	1 Lf No femoral 2 Rt All ankle pulses present Radial and ulnar pulses diminished	1 Mottled, cyanotic skin 2 Delayed blanching time 3 Hands moist 4 Temporary improvement following lumbar sympathectomy block	Rt upper thoracic sympathectomy Lf lumbar sympathectomy	1 Claudication greatly improved in lf leg and foot 2 Claudication time improved x 5 3 Rt hand warmer with good circulation	++

TABLE I—Continued  
INDICATIONS AND RESULTS OF SYMPATHECTOMY IN OBLITERATIVE ARTERIAL DISEASE

Case No	Patient	Age	Diagnosis	Condition of Extremity	Lowest Palpable Artery	Indications for Sympathectomy	Operation	Results	Late Improvement
6	E K Male Franklin 1946	26	T A O 3 yrs	1 One sq cm area of gangrene rt index finger 2 Stasis of index with elevation and delayed filling with dependency	1 Lf ulnar weak 2 Lf leg Popliteal	1 Raynaud's phenomena at onset 2 Cold clammy extremities	1 Rt upper thoracic sympathectomy	1 Increased warmth rt arm and hand 2 Healing of ulcer	+
7	J L Male SFH 38132	34	T A O 10 yrs	1 Lf 4th and 5th toes missing with draining ulcers at site 2 Rt foot cyanotic	1 Rt leg Pulses all present but diminished 2 Lf leg Popliteal	1 Cold moist cyanotic feet	1 Bilateral lumbar sympathectomy (L-2 3 4)	1 Ulcerated areas healed rapidly 2 Foot and leg warmer 3 Exercise tolerance increased x 10	++
8	A G G Female SFH 40320	14	Post traumatic spasm of brachial artery with thrombosis	1 Pulses absent lf upper extremity 2 Lf forearm and hand cyanotic cold and anesthetic 3 Induration of lf forearm muscles	1 Lf axillary	1 Cold cyanotic hand 2 Volkmann's contracture 3 Improvement with stellate sympathectomy block	1 Left thoracic sympathectomy	1 Return of pulses 2 Hand still cold and anesthetic 3 Volkmann's contracture	±
9	H L Male Franklin 4172	65	Arteriosclerosis obliterans 1 yr	1 Feet cold and moist 2 Intermittent claudication lf 2 blocks	1 No pulses below femorals	1 Cold clammy feet 2 Venous constriction with delayed blanching time 3 Improvement in color and temperature with lf lumbar sympathectomy block	1 Left lumbar sympathectomy (L-1 2 3 4)	1 Left foot warm and dry	+
10	D P Male Franklin 4123	68	Arteriosclerosis obliterans 1 yr	1 Feet cold and moist 2 Intermittent claudication rt 1 block	1 Femoral	1 Cold clammy feet 2 Delayed blanching time 3 Improvement in color and temperature with rt lumbar sympathectomy block	1 Right lumbar sympathectomy (L-1 2 3 4)	1 Right foot warm and dry	+

the control level, but was followed by the rapid development of gangrene, necessitating amputation of the leg in each case. He attributed this disaster to the opening up of the arteriovenous communications which, although it permitted the surface temperature to rise, actually resulted in still further reduction in the nutrient capillary flow.

At approximately the same time that Atlas reported his experiences, one of us had noted some curious phenomena in four cases, the significance of which was not then appreciated. The first patient was suffering from thromboangitis obliterans and had sustained an occlusion of the left iliac artery. Immediately following lumbar ganglionectomy the hypesthesia of the left foot, presumably of an ischemic nature, became much more extensive. At the time it was thought that the drop in blood pressure during spinal anesthesia and the use of the head-down position to combat this complication accounted for the manifest increase in vascular insufficiency. Some months later, however, he developed extensive gangrene of the dorsum of the foot, as shown in Figure 5, and amputation of the leg was performed. The fact that he continued to smoke and presumably had further episodes of arterial obliteration served to explain the development of gangrene, although the distribution of the necrosis on the dorsum of the foot while the toes were still viable was curious. Atlas described a similar distribution of gangrene in his cases.

The second patient was suffering from severe ischemic neuritis after an acute arteriosclerotic occlusion of the left popliteal artery. When she obtained relief from pain with lumbar block, the sympathetic ganglia were excised. The spontaneous pain which she had suffered constantly for 10 months was immediately relieved. However, oscillations at the ankle, which before sympathectomy were barely perceptible, instead of being improved, actually disappeared. The records obtained on this patient are shown in Figure 6. Necrosis of the tissues on the dorsum of the foot developed as can be seen in Figure 7, necessitating amputation of the leg three months later. The data on these four cases are given in Table II. None of these patients gave clinical evidence of increased vasomotor tone, but in each one there was temporary relief of severe rest pain following lumbar block. It is interesting to note that each of these patients had sustained an acute occlusion of a major artery, as the result of thrombosis. The terrific pain and hypersensitivity which they developed in the months following the acute occlusions might well have been due to ischemic neuritis or to some type of causalgia. In each case the relief of pain by lumbar block might better have been attributed to interruption of the sympathetic



FIG 5 — Necrosis of tissues on dorsum of foot in patient with advanced thromboangitis obliterans after lumbar sympathectomy



impulses, which is recognized to be effective in treatment of causalgia, rather than to any improvement in the supply of blood to the peripheral tissues

Atlas<sup>9</sup> has enumerated as specific contraindications to sympathectomy, 1 Severe extensive arterial occlusion, 2 Rapid blanching on elevation, and 3 Atrophy of skin and subcutaneous tissues. From our present understanding, we would now classify the cases described above as belonging to the low vascular tone group in which specific indications for sympathectomy were not present. Moreover, they presented signs which we now regard as specific contraindications to sympathectomy.

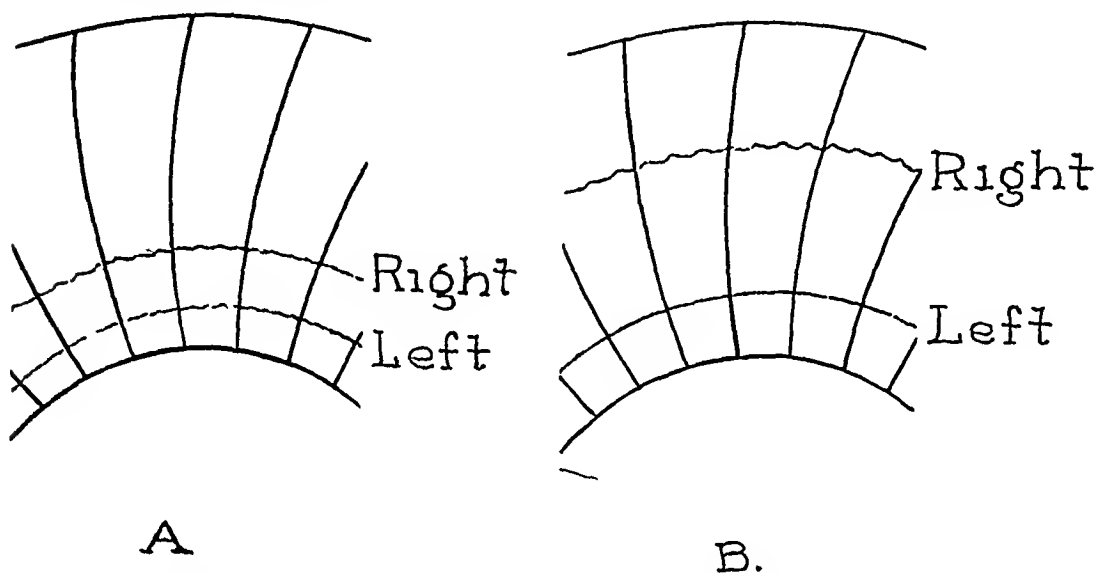


FIG 6—Simultaneous arteriograms in a patient with thromboangitis obliterans after left lumbar sympathectomy

The gangrene following sympathectomy in patients with severe obliterative arterial disease may be likened to the gangrene which so frequently follows proximal ligation of the major artery in the presence of an arterio-venous fistula. Direct measurements of intra-arterial pressure<sup>15</sup> have shown that occlusion of the major artery proximal to an arterio-venous fistula results in a precipitous drop of pressure due to the greatly expanded vascular bed available on the venous side. Arterial blood brought down by collateral pathways escapes easily into the venous side of the circulation. In obliterative vascular disease the major arteries are already blocked. Destruction of vasomotor control over the arterio-venous anastomoses by sympathectomy may abruptly deflect into the venous system the nutrient collateral flow to the capillaries. Clark<sup>4</sup> has shown that, with both the capillaries and the arterio-venous anastomoses open, there is blood available to flow through both pathways, although the relative size of the arterio-venous shunts allows far greater diversion of blood to the veins directly than through the capillaries. It is interesting to speculate on what would be the case were the volume flow of blood to be reduced by compression of the afferent arteries while the arterio-venous anastomoses were open.

TABLE II\*  
CONTRAINDICATIONS AND RESULTS OF SYMPATHECTOMY IN ADVANCED OBLITERATIVE ARTERIAL DISEASE

Case No	Patient	Age	Diagnosis	Condition of Extremity	Lowest Palpable Artery	Reason for Sympathectomy	Operation	Result	Contraindications to Sympathectomy
1	L B Male H U P 43202	45	T A O Sudden occlusion if iliac artery	Numb foot with constant burning pain	None on lf	1 4° C rise in skin temp after nerve block	Lf lumbar symp L-1, 2, 3, 4.	Immediate increase in anesthesia. Necrosis dorsum of foot Amp of leg 18 mos later	1 Absent oscillations at ankle 2 Pain due to "ischemic neuritis" 3 Continued smoking
2	E L Female Grad Hosp 149471 H U P 47754	54	Arteriosclerosis Sudden onset blanching and coldness if foot	Tender, thrombosed popliteal artery Foot warm, hypersensitive	Femoral	Relief of pain by lumbar block	Lf lumbar symp L-1, 2, 3, 4	Immediate relief of pain Necrosis dorsum of foot Amp of leg 3 mos later.	1 Atrophy of soft tissues 2 Pain due to "ischemic neuritis" 3 Rapid blanching on elevation
3	M B Female H U P 45979	59	Diabetes Arteriosclerosis Sudden occlusion if femoral artery	Foot warm but hypersensitive	Femoral	Relief of pain by lumbar block Temporary relief from periaarterial sympathectomy	Periaarterial symp femoral artery Al- L-1, 2, 3	Ecchymosis dorsum of foot Amp of leg 12 mos later	1 Absent oscillations at ankle 2 Pain due to "ischemic neuritis" 3 Rapid blanching on elevation 15 sec
4	M B Male P H 58148	58	T A O Post-traumatic causalgia.	Fracture 1-2 metacarpals Ulceration 3rd toe Foot warm, hypersensitive	Femoral	Previous femoral periaarterial sympathectomy with temporary improvement Relief of pain by lumbar block	Lf lumbar symp L-1, 2, 3.	Immediate increase in ecchymosis dorsum of foot Amp of leg 2 mos later	1 Atrophy of soft tissues 2 Pain due to "Causalgia" 3 Rapid blanching on elevation

\* We desire to express our appreciation to the following hospitals for permission to use the records from their surgical services Hospital of the University of Pennsylvania, Graduate Hospital of the University of Pennsylvania and the Pennsylvania Hospital



FIG 7 — Necrosis of tissues on dorsum of foot 3 months after lumbar sympathectomy in patient with arteriosclerotic occlusion of popliteal artery

The question may be raised as to how sympathectomy produces its admittedly good results if the only effect is the opening up of the arterio-venous communications. In the first place, the best results from sympathectomy are obtained in those patients who have capacity for vasodilatation and especially in those in whom there is a high degree of vasomotor tone. The possibility that the vasomotor tone restricts the blood flow to the tissues is suggested by the objective improvement in muscle blood flow which obtains after release of vasomotor control.<sup>14</sup> It is quite likely that even the major arteries are under vasomotor control. Arteriographic studies on three patients before and after either temporary paralysis of the sympathetic vasoconstrictor nerves or lumbar sympathectomy demonstrated an increase in the volume flow of blood through the major arteries. Figure 8 illustrates the results obtained in a patient with thromboangitis obliterans after left lumbar sympathectomy. The ankle pulses were present on both sides but after release of vasomotor control on one side the flow of blood through the major arteries was greatly increased.

It is well known that the presence of a fistula between the major artery and vein of a limb is an excellent stimulus for the development of collateral circulation. Arteriographic studies in patients with arterio-venous fistulas demonstrate the profuse development of such collaterals. The fact that quadruple ligation and excision of such fistulas is rarely followed by gangrene indicates their functional importance.

In his microscopic studies of arterio-venous anastomoses, Popoff<sup>7</sup> called attention to the frequency with which the afferent artery became dilated. It is possible that the benefits of sympathectomy may actually be attributed to the permanent opening of multiple small arterio-venous communications. Such arterio-venous fistulas furnish a stimulus for the dilatation of afferent arteries and collateral channels. Atlas<sup>9</sup> has demonstrated that, after a period of time following lumbar sympathectomy, there appears to be an actual hypertrophy of the collateral bed, allowing for an increase in the oscillations compared with those taken immediately after operation.

Although the peripheral circulation has a dual function with dual control and even a dual microscopic structure, the blood supply comes through one system of arteries. Removal of vasomotor tone by sympathectomy, especially in those cases in which this vasomotor tone is increased, may reasonably be expected to improve the circulation to the tissues in spite of the diversion of large quantities of blood through useless channels into the veins. In addition,

sympathectomy may not unreasonably be expected to furnish an adequate stimulus for the development of collateral circulation. In the presence of severe obliterative vascular disease, however, especially in those cases with low vasomotor tone, sympathectomy may be contraindicated because large quantities of

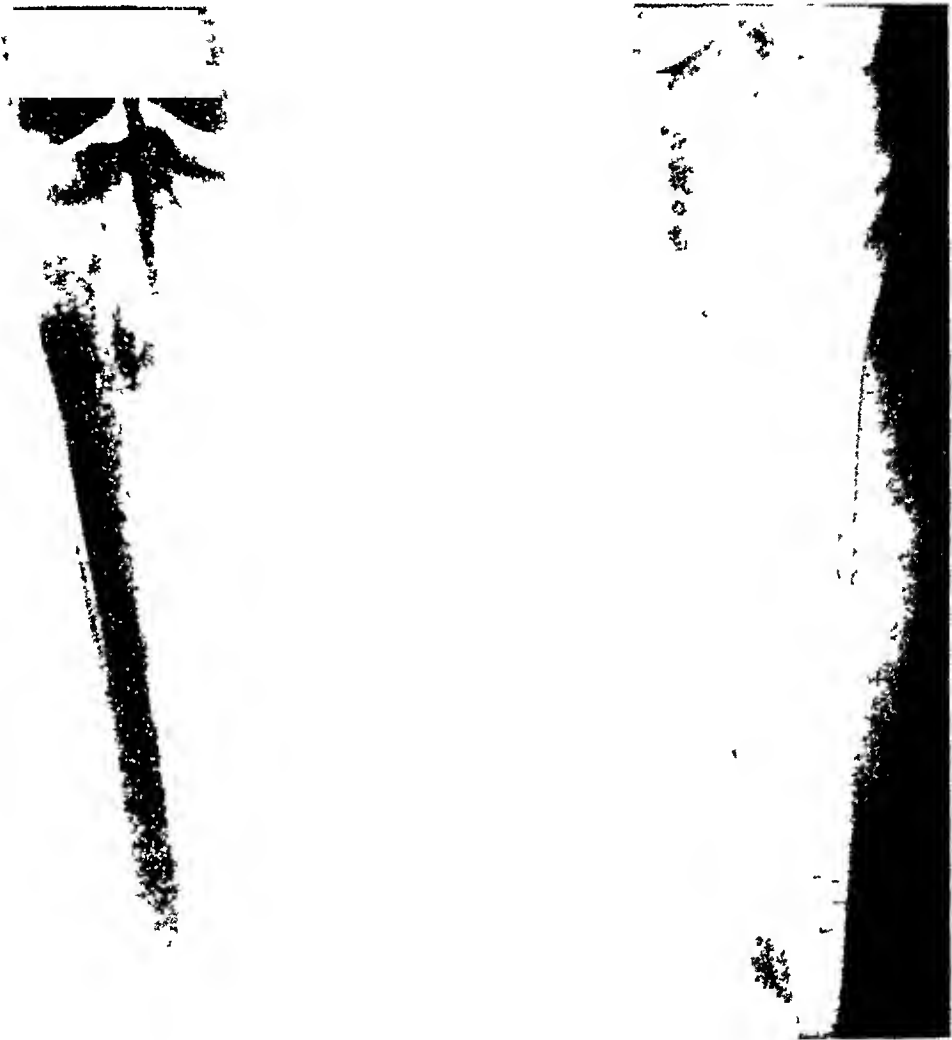


FIG 8—Oscillometric records taken at the ankle before and after lumbar sympathectomy in patient with arteriosclerotic occlusion of the popliteal artery

blood are diverted directly into the veins without passing through the capillary system

#### CONCLUSIONS

Sympathectomy is useful in the treatment of obliterative arterial disease, especially in those patients who show evidence of abnormal vasoconstriction. Even though preoperative diagnostic tests fail to show an adequate rise in skin temperature after release of vasomotor control, sympathectomy may bring about a lasting and progressive improvement.

In advanced obliterative arterial disease, however, especially in patients without evidence of abnormal vasoconstriction, sympathectomy may result in gangrene. Although the total circulation may be increased after sympathec-

tomy in these cases, much of the blood is probably shunted directly into the veins through the opening-up of numerous arterio-venous anastomoses. The nutrient capillary flow may actually be reduced.

In the less advanced cases of obliterative arterial disease, sympathectomy may promote the development of collateral circulation through permanent opening of these arterio-venous communications.

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DISCUSSION.—DR. LOUIS G. HERRMANN, Cincinnati. Doctor DeBakey has presented in modern dress another important factor in the maintenance of peripheral blood flow under various conditions. For decades physiologists have tried to impress upon us the importance of the shift of the mass of blood from one part of the body to another when certain physiologic needs are to be satisfied. The sleepiness which comes on after a hearty dinner, the cerebral ischemia which sometimes overtakes a speaker when he reaches the rostrum, the muscle cramps in extremities which come on when one goes swimming immediately after a heavy meal, are all practical examples of the shift of the mass of blood from one part to another as a result of the vasomotor function of the sympathetic nervous system.

Doctor DeBakey and Doctor Ochsner have chosen to call this the lending-borrowing mechanism, but I prefer to describe it by the term "hemometakinesia" which they have coined. I am also of the opinion that such a mechanism is of real importance and I would emphasize that such a shift of the mass of blood should be given serious consider-

ation in all patients who are to be subjected to sympathetic denervation of any part of the body

It is encouraging that vascular surgeons are also returning to the study of the fundamental physiology of the peripheral circulation and, as we have heard this morning, a better understanding and better therapy of peripheral vascular disease is our ultimate objective. The effects of local tissue hypoxia and anoxia have interested me greatly for several years and it is our hope that we may sometime add a little information about this important factor. The secondary development of venous or arterial thrombosis in patients with peripheral vascular diseases might be the deciding factor in the success or failure of any of the therapeutic agents which we employ in the management of these important clinical conditions.

Now I should like to discuss for a few minutes some of the applications of the timely studies of Doctor Freeman and his associates. It is my opinion that the operation of sympathetic ganglionectomy should not be looked upon as an innocuous procedure, particularly in patients with extensive structural changes in the peripheral arteries, since widespread denervation has been shown even to precipitate gangrene of the tissues. So far as I can determine, there is no positive evidence to show that sympathectomy does any more than relieve the increased vasomotor tone in the arterial bed and cause the opening of the arteriovenous communications of Sucquet and Hoyer in the skin. Doctor Freeman has emphasized that after sympathectomy the real stimulus to the development of a collateral arterial circulation might come directly from the opening of these small intradermal arteriovenous communications. I can only re-emphasize the fact that in patients with extensive structural changes in the peripheral arterial system unassociated with increased vasomotor tone, sympathetic denervation of the part should not be performed because the opening of the arteriovenous communications in the skin will divert large quantities of blood directly into the veins and thus reduce the nutrition of the tissues to an even lower level.

We have been interested in the effects of therapeutic measures upon the collateral arterial circulation. Doctor Freeman has already stated that sympathectomy only favors the development of a collateral arterial circulation. The flow of blood to the extremities and the exchange of blood in the capillaries, follow definite physical laws, and the importance of these factors must not be overlooked in any consideration of this kind. The flow of blood is equal to the pressure in the vessels divided by the peripheral resistance. About ten years ago we presented before this Association a physical means of increasing the flow of blood through the peripheral arteries and capillaries in patients with obliterative disease. We designated this type of treatment as "Passive Vascular Exercises." Conclusive evidence has been presented to show that the alterations of the environmental pressure about an extremity actually promote the flow of blood through existing collateral arteries. When properly used, passive vascular exercises serve as a valuable adjuvant in the management of arterial insufficiency due to structural changes in the arteries of the extremities.

Doctor Freeman's message should make us all give the problem of sympathectomy for obliterative arterial disease further serious thought and study. Such studies as these should stimulate us to give our patients the benefits of all other adjuvants which have been shown to be effective in increasing the peripheral flow of blood in such patients. Until we learn more about tissue metabolism following sympathectomy, as well as the other methods of increasing the peripheral flow of blood to tissues, we will not be able to predict accurately the effect of any of our therapeutic procedures in patients with obliterative arterial diseases.

DR. H. T. BALLANTINE, JR., Ann Arbor, Mich. Studies in progress at the University of Michigan are pertinent to Doctor Hermann's excellent discussion. Briefly, they consist of measuring peripheral blood flow in the lower extremities of normal individuals at rest and again under three varying conditions: (1) After intravenous injection of tetra-ethylammonium chloride 500 mg, producing ganglionic blockade of the autonomic nervous system; (2) After lumbar sympathetic block of one lower extremity and, (3) after injec-

tion of 500 mg of TEAC while lumbar block is still effective. Measurements of blood flow through the foot have been obtained with the venous-occlusion water plethysmograph technic. Skin temperatures have been recorded by means of the Leeds-Northrop potentiometer where feasible. Environmental temperature has been stabilized at 68 to 70° F.

The following slide is typical of our findings

- 1 Lumbar block produces a rise in peripheral blood flow and in skin temperature
- 2 Intravenous TEAC does not decrease the blood flow obtained by block
- 3 The blood pressure was not significantly altered in these normal subjects
- 4 Intravenous TEAC produces an increase in peripheral blood flow. It causes as well a rise in skin temperature equivalent to that obtained by block. This would indicate that TEAC produces a significant rise in peripheral blood flow even though the flow obtained by block is greater.

From these observations it would seem that TEAC produces a marked increase in peripheral blood flow to an extremity, despite its generalized vasodilating effect. These results have been verified in a series of 62 patients, 57 of whom showed increased flow after injection of this drug alone. This may be explained on the basis of increased cardiac output which maintains an adequate head of pressure in the arterial tree. Our ballistocardiographic studies have shown that cardiac output may rise from 10 per cent to 20 per cent after intravenous injections of tetra-ethyl-ammonium chloride.

Although changes in skin temperature are relatively the same in both procedures, there is greater increase in blood flow to an extremity with sympathetic nerve block than with TEAC. The preservation of the lending-borrowing mechanism with local block might be given as an explanation. It does not, however, fit our findings that increased blood flow to the foot produced by paravertebral sympathetic block is not decreased by an injection of TEAC. These results indicate that generalized vasodilatation and possible abolition of the lending-borrowing mechanism does not inhibit increased blood flow to a local part, provided cardiac output can be increased sufficiently to maintain arterial pressure.

A more probable explanation for the disparity between the increase in blood flow after block and after injection of TEAC is that in 500 mg doses the drug does not produce complete autonomic block.

DR I RIDGEWAY TRIMBLE, Baltimore. Doctor Freeman's paper is most timely in pointing out the pitfalls that may be encountered in surgery of the vascular diseases. Some years ago, before the war, we wrote about some of these cases in which the tests were not conclusive, yet beneficial results did follow operation. This has been borne out by DeTakats, who says he is in agreement, and he is now submitting patients to operation who, according to tests, were formerly considered unsuitable. I have never encountered gangrene of the extremity following lumbar sympathectomy.

Doctor DeBakey's paper is most interesting. Hematokinesia—the borrowing-lending mechanism, better known as Greco-Turkish mechanism of lend-lease. We have recently used this principle of borrowing blood for a double purpose, to prevent shock at the time of operation and to decrease the incidence of postoperative thrombosis.

The skin surface of the lower extremities comprises 38 per cent of the total body surface. It is the blood from this large area that we wish to borrow for use elsewhere.

Dr David Lynn and I are now investigating the possibility of lowering the incidence of postoperative thrombosis and thrombophlebitis by binding the lower extremities with elastic bandages during operation and by keeping these bandages in place after operation for a period of two weeks. We are at present conducting studies on the blood flow in the deep veins of the lower extremities after the application of these bandages.

DR D W GORDON MURRAY, Toronto. I should like to comment on the papers of Doctor Smith and Doctor Blakemore. Doctor Smith in his paper described using plastic

tubes for anastomosis I would like to ask Doctor Smith if he lined the tubes with a venous graft or was the anastomosis done with the plastic material only

Regarding Doctor Blakemore's paper, I admire the way he puts this damaged artery together My own predilection would be for suture, but that is a weakness on my part The maintenance of circulation after either graft or suture, I think, is the main thing to be obtained The main thing is to provide circulation to the area involved In my hands, by giving heparin I can be more certain to maintain the patency of the anastomosis

In one of the animals' hearts shown yesterday, removed from an animal in which we had done a vein graft in a carotid artery nine years previously, the vein graft was removed at this time Its lumen was patent It was slightly larger than the adjacent artery The wall in some places was rigid so that it fractured when it was opened out I am not sure whether it was calcium or bone Further investigation of this will be made and sections made to determine just what are the changes in this venous graft after nine years functioning in an artery

In a clinical case, a boy in whom a 2.5 inch graft of vein was placed in the femoral artery eight years ago, this has been working well ever since There is no sign of aneurysm On palpation it does not feel rigid or stiff It seems to be functioning satisfactorily

There probably is a place for venous grafts in arteries under suitable conditions

DR PETER HEINBECKER, St Louis I want to discuss Doctor DeBakey's paper, and to ask Doctor Ballantine a question The alteration of blood flow to organs and tissues in response to need is a dynamic phenomenon dependent on nervous, humoral, local metabolic and thermal influences Of these the accumulation of local metabolites probably is of first importance It is not necessarily dependent on the sympathetic nervous system for its initiation or continuance This is supported by evidence of its adequate functioning in the denervated extremity Of the important humors, none is more so than epinephrine, which serves to decrease the blood flow to the skin and the splanchnic area while increasing that to the muscles, the brain and the heart For the release of epinephrine the sympathetic nervous system is essential The nervous influences which modify blood distribution are reflexly initiated They serve particularly in the maintenance of a stable blood pressure and a normal body temperature In special situations nervous influences modify secretion rapidly in response to need, a function later taken over in large measure by humors or enzymes

The temporary increase in the size of a portion of the vascular tree effected through denervation is a static phenomenon, not to be confused with the dynamic processes involved in blood distribution occurring spontaneously to meet changing metabolic requirements

I was much interested in Doctor Ballantine's statement that tetra-ethyl-ammonium chloride causes a block in the ganglia of the autonomic nervous system I would like to know what evidence he has of such a block

DR WALTER G MADDOCK, Chicago I would like to comment first on the paper of Doctor Freeman It has been pointed out before that the skin temperature response of the hands and feet to an increased environmental temperature or to a sympathetic or peripheral nerve block is greatest in the normal individual, for his unobstructed vessels can dilate to the maximum From work done with Doctor Collier at Michigan the old theory was re-emphasized that the arms and legs, particularly the hands and feet, play a very important part in the dissipation of heat from the body, being the areas of greatest variation in superficial blood supply in response to heat production versus the environment into which the heat has to be dispersed The hands and feet act in the same way as the radiator of an automobile The engine block gives off heat, like the body, but the shunt of water to the radiator is the main variant as the need for heat dissipation varies Doctor Freeman has shown again the arteriolar-venous shunt system in the fingers and toes, which un-



doubtedly is a part of the mechanism for passing more blood through these areas when there is a need for more heat dissipation. With the greatest responses in the normal, one must be careful then to not interpret all increases in peripheral skin temperature as a result of test procedures as an overcoming of "vasospasm." Much of the temperature increase is due to an overcoming of vasoconstriction which is a normal part of the heat dissipating mechanism. In actual practice one often does not need to test for vasospasm but can see its presence by sweating or multiple color changes in the part.

So far as sympathectomy is concerned, particularly for the lower extremities, it is a relatively simple procedure now and I place it under the heading of conservative treatment. Patients with a peripheral vascular deficiency from arteriosclerosis are debilitated and disabled just as much as a cardiac patient, and every method must be used to improve the blood supply to the legs and feet. A slight gain may be sufficient to enable them to carry on for months or years without trouble. And since gangrene is such a common end result in all patients with serious peripheral vascular deficiency, it is difficult to be certain that in some way the sympathectomy caused or hastened this death of tissue. I do not believe that Doctor Freeman is advising that we abandon sympathectomy for many of these patients.

Doctor DeBakey's paper on "lending-borrowing" blood from the body proper to the extremities in cases of need is interesting. The lending-borrowing should be brought about in the conservative management of all cases of a peripheral vascular deficiency. If normal individuals keep their trunk warm by wearing woolen underwear, then more blood will be sent to the hands and feet for the dissipation of heat. Patients with peripheral vascular deficiency as a result of peripheral arteriosclerosis or Buerger's disease should be instructed to keep the body warm at all times, to wear woolen underwear and woolen socks if necessary, for more blood will then be sent to the extremities. Such patients in the hospital should be kept extra warm, not just comfortably so; the body should be warmer than usual, to a point a little short of sweating. Extra blankets should be supplied, or a heat cradle placed over the abdomen, not over the feet. An electric pad to the abdomen will also add general heat, and one of the new electric blankets is a suggestion. In contrast to many other forms of treatment, such environmental therapy sending blood to the extremities can be used in the hospital for 24 hours a day, an essential time period to combat the disease and disability of peripheral vascular deficiency.

DR FRANK B. BERRY, New York: I would like to discuss Doctor Smith's paper and to add our own experience. We were fortunate in having some experience behind us, so that when the Seventh Army prepared to go into France we sent out a directive requesting that all major injuries of arteries be listed. We had 1086 such cases.

Further amputations undoubtedly were necessary in the general hospitals, but we urged that all such injuries be held in forward hospitals until the outcome was known. Our femoral artery injuries are not subdivided but are dealt with as a group. We had 190 cases, 90 amputations; we had 179 popliteal injuries, 125 amputations. In Tunisia, for example, the Ninth Evacuation Hospital had nine injuries of the popliteal artery, resulting in 100 per cent amputations. In France they had three consecutive cases with no amputations. That is how these injuries varied as to outcome. Much depended on the type of wound, extent of soft part damage, coexisting fractures, time elapsed between wounding and surgery, etc.

We did use some heparin and we considered that it helped. We used glass and plastic tubing, and some of the hospitals had Blakemore cuffs and used grafts. We believed these were all helpful when it was possible to use them.

It has been advocated in the case of elderly people in whom there is lessened arterial supply to the leg, that a bilateral sympathectomy be performed. Doctor DeBakey's lending and borrowing mechanism may suggest that. We know that these people are prone to go on after sympathectomy has been performed on one side to develop gangrene in the other leg, and we wonder in these cases if a bilateral sympathectomy may not be indicated.

DR. ALTON OCHSNER, New Orleans My remarks will be limited to a discussion of Doctor Freeman's paper I am sure that Doctor Freeman did not wish to leave the impression that older patients with arterial disease should not be given the advantage of sympathectomy. We have become increasingly more impressed by the desirability of resorting to sympathectomy even in older persons who have obliterative arterial disease and, although in not all of these patients can the extremity be salvaged, the salvage incidence is about 75 per cent, which makes the procedure justifiable We have also learned that the results obtained by temporary blocking of the sympathetic nerves by novocaine will not give a true indication of what can be obtained by sympathectomy in these older individuals We have had considerable experience with sympathectomies in older individuals with obliterative arterial disease, and in only one instance have we observed a gangrene which apparently became progressive after the sympathectomy We believe that this was coincidental and that the sympathectomy was not in any way associated with the gangrene but that the gangrene occurred in spite of the sympathectomy There are many other patients in whom gangrene has been prevented by a sympathectomy It seems to us that to deny an older patient any procedure which will increase his chance of maintaining a viable limb would be extremely undesirable

DR WILLIAM F MACFEE, New York Doctor Smith's observations on the treatment of injuries of major arteries during the war are impressive It is obvious that they represent the general experience of World War II It is also evident from his report and other records that current methods of restoring continuity of severed vessels, while occasionally successful, have not been sufficiently so to materially alter results I do not believe we can claim that the results of new methods, which include the bridging of defects between severed ends, are superior to the older procedure of simple ligation

The failures no doubt have been due in part to defects in the methods employed, but perhaps in greater measure to the character of the wounds The energy, or in this case the destructive force of a missile, varies directly with its mass and with the square of its velocity The destruction of tissue produced by the modern high velocity bullet or shell fragment is enormous An artery is not simply cut, but as a rule a segment is torn out and a large area of surrounding parts, including the collateral circulatory system, is reduced to a pulplike state and completely devitalized In addition to the local wound, frequently there are other grave wounds of the same extremity or of other parts Under such circumstances, it is not surprising that so many limbs are lost, but rather that something like 50 per cent are saved

To obtain better results it is evident that better methods of repair must be found. A serious disadvantage in dealing with war wounds is the impracticability of using the anti-coagulants Doctor Berry has described a case of delayed hemorrhage which illustrates the danger of interfering with the clotting mechanism in the presence of extensive wounds Unless better methods of local hemostasis can be found, it would appear that any reliable method of restoring the continuity of major arteries interrupted by war wounds must preclude the use of anticoagulants

DR. FREDERICK L REICHERT, San Francisco Perhaps I did not understand Doctor Smith, but in the last war they tied off the corresponding named vein when the artery was severed I do not know why that was not done in this war

That case of gangrene Doctor Freeman showed I think is due to thrombosis of the femoral vessels, and has nothing to do with sympathectomy If you want to treat these people with impaired circulation you should consider the entire atherosclerotic condition I consider five extremities, including the head, and you have to keep that as warm as you do the legs and arms Sympathectomy has helped these people, up to the age of 80 or 90 I think this case of gangrene is due to thrombosis of the femoral vessels and not to sympathectomy

DR. RUDOLPH MATAS, New Orleans I believe that Doctor Blakemore's restoration of the main arterial channel in the aneurysmal sac by his "vein graft inlay" is a decided

step forward in the practice of conservative aneurysmorrhaphy, specially in dealing with those aneurysms in which the reliability of the collaterals is in doubt

Despite the fact that in the majority of cases in which a pulsating hematoma has had time to develop as an aneurysmal sac, thereby assuring the establishment of a collateral circulation, and that the limb will be preserved even if the sac itself is obliterated,—the restoration of the main channel of the circulation in the sac is desirable, since it is possible that the collateral circulation may be preserved sufficiently to save the limb from an amputation, but not sufficiently to prevent secondary ischemic atrophies and other functional disabilities which leave an imperfect cure

It is fortunate that in the vast majority of the endoaneurysmorrhaphies of the obliterative type, the collateral circulation is so little disturbed that secondary ischemic relics of the obliterative aneurysm are seldom sufficiently apparent to impair the cure. Nonetheless, it is obvious that, when the anatomic conditions within the sac are not favorable for the restorative types of endoaneurysmorrhaphies (Endo-A, Restorative, Endo-A Reconstructive) that the use of a Blakemore venous lined vitallium tube or a plain venous inlay with his vitallium cuffs would be a helpful and relatively simple resource

It is well to remember that in trying to restore the continuity of the main artery in the sac of the aneurysm, the Blakemore procedure is not applicable to all type of sacs, but seems to me specially adapted to sacs in which the inlet and outlet lie in the floor of the sac in the same horizontal level, as is more frequently the case in popliteal aneurysms. It is different, however, when the artery lies on the roof of the sac and the outlet appears on the floor, or when the inlet and the outlet are eccentrically placed at different levels. To adjust a venous graft under these conditions may involve too much traumatism and handling to make the graft a success. These differences in the relation of the artery to the sac I described long ago in connection with the "Morphology and architecture of aneurysmal sacs" and in the interpretation of "Rotation in aneurysmal sacs," specially those of the popliteal space (Keen's Surgery, Vol V, pp 221-226)

While great progress has been accomplished within the course of the half century since I began to utilize the suture as a conservative substitute for the ligature in the cure of aneurysms—so that now the repair of injured arteries and veins has become a sort of plastic art in which many of our younger contemporaries have become great artists—I believe that we are on the way to devise still simpler methods and more handy materials than venous grafts, to bridge over gaps in the arterial stream. The distance we have travelled on the road of progress, between the Tuffier tube of the first world war and the venous lined vitallium tube of the Blakemore pattern—is quite encouraging

Doctor Smith's study of 114 arterial wounds followed by gangrene in 54 per cent proves that the disastrous injuries of the great vessels at the front fully justify the special care and concentrated attention that the Surgeon General's office has given to these wounds in the second world war, in a supreme, but yet feeble effort to counteract the ever increasing destructiveness of the implements and materials of warfare

Doctor DeBakey and associates and Doctor Freeman have dealt with the Surgery of the Sympathetic very interestingly, but from an entirely different viewpoint. Doctor DeBakey has opened a new field of therapy for the play of the already crowded vasomotor nerves which may soon yield a crop under Doctor DeBakey's fertile sowing

Doctor Freeman has rendered a real service by sounding a note of alarm regarding the indiscriminate resort to lumbar sympathectomy by operation or by anesthetic block, without clear differentiation of the indications and contraindications of the procedure

What is particularly objectionable is to resort to lumbar sympathetic block as a routine procedure before or after an operation for an aneurysm or a main artery injury in the extremities, in which there is no question regarding the sufficiency of the collateral circulation. There is, no doubt, an enormous abuse of this serious procedure, particularly when performed by inexperienced and incompetent assistants who, at best, simply perform a paravertebral novocain anesthesia. As a rule, no trouble is taken to demonstrate the effectiveness of the injection by the temperature of the dependent parts or determine, in

other ways, if the anesthetic has actually reached the ganglia. It is interesting to note in this connection that Doctor Elkin with all his large experience in aneurysmal surgery, has gotten along altogether without a single call for a lumbar block. In my experience, in over 600 operations on the surgical blood vessels, including 250 aneurysms, I have only once called for the "lumbar block" in threatened gangrene of the foot. It is more than probable that, if sympathetic lumbar block had been in vogue when I was operating, in earlier years, as it is now, I would probably have been doing Sympathectomies *a la mode*. I wish it understood that I prize sympathectomy as a precious help when it is needed, but object to it as a routine prophylactic for unthreatened gangrene.

The same protest applies against the abuse of transfusion, which is now being used as a panacea for all evils and especially as a prophylactic against shock and hemorrhage in operations in which there is no reason to expect such complications. There is no doubt that in this way much good blood is wasted, and many who are only profiteers and not patients, benefit by the procedure.

I have long trespassed upon the indulgence of the Chair and must now close with thanks to him and to the vascular surgeons who have contributed so brilliantly and profitably to the enjoyment of the Scientific Program.

DR ARTHUR H. BLAKEMORE, New York (closing). I am deeply indebted to Dr. Rudolph Matas for discussing my paper. More than 50 years ago he presented to the profession an operative technic for the cure of peripheral arterial aneurysm that has greatly lowered the incidence of gangrene. Doctor Matas' teachings were ever before us in evolving the vein graft in lay technic. Therefore it is with some satisfaction that I present this method which does not violate his teaching in necessitating removal of the aneurysm sac, as have former methods of vein graft bridging for the restoration of blood flow.

Doctor Murray has asked about the use of heparin. We employed it postoperatively in all four cases.

DR. M. E. DEBAKEY, New Orleans (closing). I should like first to express my appreciation of the stimulating discussion. In view of the political implication of the term, "borrowing-lending," it is perhaps well that a more scientific term has been proposed for this phenomenon.

I was particularly interested in Doctor Heinbecker's comments concerning cardiac output and its effect upon the changes in peripheral blood flow which we have described. It is somewhat difficult, however, for me to understand how variations in cardiac output can produce concomitantly changes of a different order in the volume of blood in such peripheral parts as the fingers and toes. In other words, I do not understand how an increase in the volume of blood in the toes associated with a simultaneous decrease in the volume of blood in the fingers may be attributed to fluctuations in cardiac output.

Doctor Ballantine's comments regarding recent studies which they have done, showing an increase in cardiac output following the administration of tetra-ethyl-ammonium chloride are also of interest. As we have indicated previously, an increase in cardiac output can produce an increase in blood flow to peripheral parts which, obviously, should be generalized. The desirability, however, of producing an increase in blood flow to a peripheral part by this means is, I think, open to question.

With regard to Doctor Berry's question concerning bilateral sympathectomy, especially in certain forms of peripheral vascular disease involving the lower extremities, we have come to employ the procedure with increasing frequency.

DR. MORRIS K. SMITH, Staten Island, New York (closing). In answer to the question as to whether the plastic tube was lined with vein, it was not. Some surgeons used glass tubes. Plastic tubes have the advantage of being malleable when heated. Doctor Murray has shown that heparin opens the field for arterial repair.

Doctor Berry quoted from the experience of the Seventh Army and said that doubtless many cases came to amputation after evacuation. I did not use our amputation rate in my figures because so many patients with limbs becoming gangrenous had to be sent on before we felt they were ready for amputation.

Doctor MacFee brought out a salient feature in arterial injuries of war, the widespread destruction caused by modern missiles. A reason the incidence of gangrene is so high is injury to the collateral circulation. If we are to have better results in future wars it is important to develop some means of preserving the main blood channel. Heparin will keep the anastomosis open if it can be used. It may be possible to close wounds more completely than we do in the average case in order to make heparin less dangerous.

Doctor Reichert raised the question of ligation of the accompanying vein. The data in my files are not sufficiently detailed to give an answer. It is to be remembered that when the artery is wounded the vein also is likely to be and therefore to require ligation.

DR NORMAN E. FREEMAN, San Francisco (closing). I appreciate very much the comments which have been made in the discussion of the place of sympathectomy in the treatment of obliterative arterial disease.

In regard to Doctor Reichert's objection, since the patients already had obliteration of their femoral arteries it is unlikely that thrombosis of the femoral vessels accounted for the gangrene after sympathectomy.

In reply to Doctor Maddock and Doctor Ochsner, we are not abandoning sympathectomy in patients of the older age group. In fact, we are actually advocating an extension of this valuable procedure. We believe, however, that arterial ischemia *per se* is not an adequate indication. We think that there is a specific indication for the performance of this operation. The indication is evidence that *abnormal* constriction of the blood vessels exists. In the absence of this indication there may be specific contraindications to sympathectomy. When contraindications are present, widespread denervation of the vascular bed may actually result in harm. We have simply called attention to a possible mechanism through which the nutrient supply of blood to the tissues may be reduced by sympathectomy.

It must be emphasized that this concept is still hypothetical. Diversion of arterial blood into the veins as a result of sympathectomy still remains to be proved in patients with peripheral vascular disease. Fundamental investigations by numerous individuals have established certain mechanisms which may be involved. Such mechanisms appear to explain the unfortunate results which we have occasionally observed.

## CHONDROSARCOMA\*

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PHÉMISTER described chondrosarcoma of bone in 1929 as a distinct clinical and pathologic entity<sup>11</sup> This group of neoplasms has since been included in the classification of osseous tumors by the Bone Sarcoma Registry of the American College of Surgeons<sup>3</sup> Reports of chondrosarcomas antedate Phémister's contribution but his efforts focused the attention of American surgeons and pathologists on these lesions The 13 cases seen by us during the past 20 years not only illustrate the general characteristics of the group but also emphasize certain difficulties in pathologic diagnosis, surgical treatment and prognosis We have also reviewed 61 cases from the files of the Bone Sarcoma Registry

Chondrosarcomas may arise in any bone that grows by endochondral ossification The sites most frequently involved are the ends of the femur and tibia, the proximal end of the humerus and the pelvis These locations account for 75 per cent of the 74 chondrosarcomas we have studied

Chondrosarcomas may arise either centrally or peripherally They form bulky masses which invade and destroy adjacent bone and project into the surrounding soft tissues They are among the largest neoplasms encountered Their external surfaces may be smooth or bosselated They look gray and feel firm although large areas may be elastic and even fluctuant, depending upon the extent of liquefaction necrosis and the amount of myxomatous tissue present Hard areas usually indicate calcification A part of the tumor may appear encapsulated on superficial examination but closer inspection reveals that it is merely circumscribed by distended periosteum Infiltration of soft tissues may be seen macroscopically and atrophy of contiguous skeletal muscle is commonly found

One usually has no difficulty in recognizing the hyalin, blue-gray translucent cartilage that is seen on cut section of most chondrosarcomas It may be lobulated by thin fibrous septa but frequently lobulations are indistinct and sometimes, absent Islands of myxomatous tissue appear pale and watery Ragged, crateriform excavations filled with viscous fluid are found in some tumors Irregular deposits of pale yellow, opaque, gritty, hard material indicate calcification, a common finding Some of the tumors may contain relatively small fibrous appearing areas and true bone is sometimes found

The microscopic anatomy of chondrosarcoma is extremely variable Each tumor may mirror the complete histogenesis of cartilage, or the end product of tumor differentiation may contain only one histogenetic phase The more cellular and more anaplastic areas are usually encountered at the periphery of the

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tumor The center is frequently necrotic, calcified or ossified Ovoid lacunar cells predominate in typically hyalin areas, spindle-shaped or stellate cells, in myxomatous foci Extreme pleomorphism may characterize some tumors or parts of an individual neoplasm Matrix may be basophilic and hyalin, amorphous and foamy, acidophilic and fibrillar or completely absent The amount of matrix varies inversely with the degree of cellularity Lichtenstein and Jaffe<sup>8</sup> have stressed the importance of detailed cytologic study in the diagnosis of some chondrosarcomas We agree in general with their tenets The cells of malignant cartilaginous tumors regardless of type contain relatively large nuclei which may be either granular, vesicular, compact or hyperchromatic Cytoplasm is homogeneous, granular or vacuolated Binucleate cells are present, often in large numbers Multinucleated forms and even true tumor giant cells may be found in some chondrosarcomas Mitotic figures are usually not present in high concentrations Vascularity varies widely Most of the blood vessels are contained in the pseudocapsular tissue and follow septa into the substance of the tumor It is extraordinary how few viable blood channels may be seen in some huge chondrosarcomas while other, considerably smaller, may contain highly vascular areas One occasionally sees endothelial lined spaces completely surrounded by neoplastic tissue We have gained the impression that more vascular chondrosarcomas metastasize more readily than those in which vascularity is not conspicuous This may be related to the tendency for these neoplasms to invade veins and form tumor thrombi

Chondrosarcomas affect men more often than women They occur relatively later in life than the more malignant osteogenic sarcomas The mean age of the 74 cases studied was 38 years, the youngest 13, the oldest 67 It is difficult to estimate the real duration of these tumors because many of them give little evidence of their presence and some are obscured by their anatomic location Only three of our patients had symptoms for less than a year The average duration of symptoms in the other nine was 4.5 years but this is heavily weighted by those people with recurrent tumors The majority of all the cases we have studied had symptoms for more than 12 months before they sought treatment Pain or a mass are the common complaints Pain is mild and intermittent at first but increases in intensity and becomes constant over a long period of time The lesion is usually extensive when a patient complains of both tumor and pain Physical examination reveals little unless a palpable mass is present There is occasionally a sensation of increased warmth over these tumors, some even appearing inflammatory Other findings are due to the mechanical effects of the tumor by limiting motion and impairing function

On roentgenographic examination chondrosarcomas form poorly delimited, bulky masses The central lesions, as Phemister noted, produced expansile swelling of the shaft which may be associated either with thickening or dissolution of the surrounding cortical bone<sup>11</sup> Peripheral chondrosarcomas excavate the bone but are rarely associated with visible evidence of periosteal bone formation The bulk of the tumor is extra-osseous Focal areas of calcification, when present, produce small, irregular, fuzzy blotches and streaks of increased

density Occasionally chondrosarcomas have a bony pedicle We interpret this as presumptive evidence of pre-existing osteochondroma Involvement of joint spaces is distinctly rare although most of these tumors arise near the ends of long bones and extend in their long axes

Chondrosarcomas vary widely in their growth potentialities Some remain well localized despite multiple recurrences Others metastasize widely within a relatively short time The difficulties encountered in estimating the prognosis of chondroid neoplasms and the effects of surgical therapy are best shown by specific examples

The first four cases to be reported, Nos 1 to 4 incl, had chondrosarcomas in the extremities where clean cut amputation could be performed well away from the growths Case 4 was associated with Ollier's disease and multiple hemangiomas Despite the multiplicity of benign chondromas only one malignant cartilaginous tumor has been found All of these patients have remained well without recurrence for at least six years, and are undoubtedly cured

The protracted course of some relatively indolent forms of chondrosarcoma are exemplified by the next three cases, Nos 5, 6 and 7 The initial operation in each case was inadequate Recurrences followed but no evidence of metastasis was ever found although the recurrences grew more rapidly and appeared more anaplastic than the original tumors

The eighth case was a sacral chondrosarcoma inoperable from its inception It produced peritoneal implants with fatal issue 20 months after the onset of symptoms

With Case 9, there were three cartilaginous tumors The one in the pelvis was malignant It recurred after partial excision and eventually metastasized to the lungs The histologic appearance of the chondrosarcoma was less distinctive than usual Even the metastases lacked the usual cytologic features of chondrosarcoma We cannot eliminate the possibility that each of the masses described represents an individual neoplasm unrelated to the others This, however, seems improbable

Case 10 is a more highly malignant type of chondrosarcoma than any of the previous ones A large cartilaginous tumor containing small areas of undifferentiated pleomorphic sarcoma was excised from the ilium Metastases developed soon afterwards

Interinnomino-abdominal amputation would seem to offer a better chance for cure of chondrosarcomas of the pelvis than would local excision The following cases were huge tumors removed by hind-quarter section The results are disappointing Cases 11 and 12 have been reported previously in more detail<sup>9</sup> Cases 7 and 10 might have been salvaged by hind-quarter amputation but circumstances were such that this operation was not advised

Not all bulky cartilaginous tumors are malignant The last case (Case 14) was a huge chondroma arising from the tibia It was recognized and removed locally with a successful outcome

There are two factors responsible for our poor results The first is improper evaluation of the malignant potentialities of some chondroid tumors, the sec-



ond, inadequate surgery The differential diagnosis between chondroma and chondrosarcoma may be difficult

Chondrosarcomas may appear encapsulated on macroscopic examination but we have not seen any instance in which a distinct capsule intervened between chondroid tissue and adjacent cancellous bone On the contrary, invasion of the marrow spaces was demonstrated histologically in each case Perhaps this accounts for the poor results following curettement or excision One is loathe to sacrifice more bone than seems necessary and macroscopic examination fails to reveal the true extent of the lesion within bone Our experience indicates that benign cartilaginous tumors are well circumscribed if not completely encapsulated We have not observed invasion of the spongiosa by neoplastic cells in those chondroid lesions which responded favorably to curettement It would seem that local recurrence in bone may be a reasonably good criterion of at least locally malignant chondrosarcoma unless strong evidence to the contrary can be adduced When such a recurrence is noted a radical removal of the area is indicated if there is to be a cure

There is little that can be seen on the cut surfaces of some chondroid tumors that might lead one to suspect their malignant character Both chondrosarcomas and chondromas may be bulky Both may be lobulated Both may contain gelatinous, cystic or calcified areas Chondrosarcomas, however, seem to be more destructive Eccentrically placed chondrosarcomas reduce the affected bone to a melange of gritty and hyalin material in which the outline of the bone is seldom retained Both central and peripheral types tend to extend in the bone's long axis

A final determination of the status of a given chondroid lesion must rest on consideration of *all* the facts Histologic examination is extremely important and particularly the cytologic characteristics stressed by Lichtenstein and Jaffe<sup>8</sup> The pathologist's examination must be thorough Many sections are essential Close inspection of multiple cut surfaces sometimes reveals small fibrous-appearing areas containing tissue totally different in histologic character from the tissues comprising the more bulky part of the neoplasm

We have found no absolute histologic or cytologic criteria which distinguish the locally invasive chondrosarcomas from those that metastasize to distant organs other than the foci of frank osteogenic sarcoma encountered in only two cases The character of the matrix seems to be of little importance Myxomatous tissue has no evil connotation in our experience Bloodgood reported benign myxomas of bone that responded favorably to conservative surgical measures;<sup>1</sup> We have had similar experience Certainly the more aggressive chondrosarcomas seem to be more cellular than those that remained well localized A great variety of cell types were found among these neoplasms and in individual members of the group No correlation of type of cartilage cell with biologic behavior seems possible The single most constant change that characterized the group was the presence of relatively large nuclei in most of the cells The nuclei were either granular or vesicular and attained maximum diameters at least one half that of the cells in which they lay This contrasted

sharply with the small pyknotic nuclei commonly less than one-third the greatest cell dimension seen in most chondromas. Binucleate cells were seen in all of the chondrosarcomas. Tumor giant cells were a distinctly evil omen. Mitotic figures were found rarely among cartilage cells in the great majority of our cases.

The two patients whose metastases contained no cartilaginous elements are particularly interesting. Had tissue for histologic examination been taken only from the bulky 90 per cent of these tumors their true nature would have escaped detection. In Case 12 the significant area was obscured by cartilage that overlapped the hip joint. Even the tumor component that invaded the medulla of the femur was frankly chondroid. It is possible that some of this patient's metastases may have contained cartilage but permission for post-mortem examination could not be secured. The second patient's tumor (Case 10) contained multiple foci of highly anaplastic sarcoma imbedded in frankly cartilaginous neoplasm. No cartilage has been found in any of the metastases yet examined. There are a number of cases recorded in the Bone Sarcoma Registry in which obviously chondroid neoplasms fulfilling the modern criteria for the diagnosis of chondrosarcoma developed metastases that contained spindle cell and/or osteogenic elements but were devoid of recognizable cartilage. We believe that the prognosis among patients whose chondrosarcomas contain foci of anaplastic fibrosarcoma or histologic osteogenic sarcoma, however small, is much less favorable than in those whose tumors contain only recognizable cartilage or its precursors. One may argue that there is little difference between these two cases and the more readily apparent osteogenic sarcomas. We would point out that osteogenic sarcomas as commonly denoted are tumors affecting younger individuals. Frank osteogenic sarcoma among older people is usually associated with osteitis deformans. Another important difference is the slowly progressive character of the lesions. This is shown particularly well in Case 12 who was known to have had a cartilaginous neoplasm for at least six years. The other example is less convincing although it seems incredible that the neoplasm found at operation could have been present for only the four months indicated by the history. This tumor arose in an inaccessible location where a large mass could easily escape detection for a long time and might easily fail to produce symptoms.

There is little doubt that highly malignant chondrosarcomas may evolve from benign cartilaginous tumors<sup>4, 5, 8</sup>. We found no absolute proof of a pre-existing benign lesion among any of our cases yet there is good evidence of changes in the structural characteristics of individual tumors over long periods. In at least two patients multiple sections from the first tumors available for study failed to reveal unequivocal histologic evidence of chondrosarcoma. The patterns seen were identical with those found in some phalangeal chondromas which responded favorably to simple curettement. It is possible that a nidus of more anaplastic tissue escaped detection. We do not think so. The recurrences in each instance were more clearly sarcomatous than were the parent tumors. In some cases the recurrences became progressively more anaplastic.

over a period of time. It should be recalled that surgery altered drastically the natural habitat of the tumor cells affecting their relationships with other tissues and particularly their blood and nerve supply and their lymphatic drainage. We would suggest that competition for survival required the development of new characteristics by the neoplastic cells which were reflected in their growth potentialities and morphologic features. Supporting evidence for this contention is found in the work of Spencer and Calnan<sup>12</sup> and Earle.<sup>2</sup> The situation seems to be exactly analogous to the well-known development of neurogenic sarcoma after repeated incomplete excisions of recurrent neurofibromas.<sup>4</sup> There can be little doubt that chondrosarcomas may evolve "spontaneously" from pre-existing chondromas or osteochondromas. It seems probable that inadequate surgery may contribute importantly to such a sequence of events.

Surgery is the only effective means of treatment of chondrosarcomas. Roentgen therapy may relieve pain but seems to be totally incapable of reducing appreciably the size of the mass in therapeutic dosages. We advise amputation for chondrosarcomas of the extremities. A wide zone of normal tissue must intervene between the lesion and the line of amputation if the procedure is to be successful. This may seem unnecessarily radical in those cases where the cytologic characteristics are the only findings that indicate a malignant tumor. Our decision is based on a comparison of end results of surgical treatment of tumors situated in the axial and appendicular skeletons respectively. We found that most types of chondrosarcoma arising in the pelvis recurred after curettage or wide excision whereas histologically similar neoplasms affecting the extremities were usually cured by clean-cut amputation. There is hope for patients even with large tumors of the pelvic bones or the trochanteric region of the femur but interinnomino-abdominal amputation is a formidable operation. Our poor results suggest that hind-quarter section should not be delayed until everything else has failed. Gordon-Taylor's<sup>7</sup> and Pack's<sup>10</sup> experience lends support to this opinion. For practical purposes it may be wise to excise or curette a suspicious chondroid tumor but the experience of Ghormley and Meyerding<sup>6</sup> does not support this. If unequivocal evidence of chondrosarcoma be present further treatment will probably be essential. We recommend that this be carried out at once in those patients whose neoplasms are poorly differentiated. The well differentiated tumors may be expected to recur locally before metastasizing. It would seem, then, that more radical procedures can be delayed safely until recurrence has confirmed the diagnosis.

#### CASE REPORTS

Case 1.—F. R., No. 141241, a man age 58 was admitted to Strong Memorial Hospital June 8, 1938. Six months ago he bumped the middle finger of his right hand on a barrel. It did not swell or pain much and did not prevent him from working. Two months ago the finger had a lump on the dorsum at the distal end of the proximal interphalangeal joint. The joint was stiff. There had been a gradual painless enlargement of the finger.

*Examination* showed a greatly enlarged middle finger with a fusiform bony and rubbery-feeling growth. This was a tumor of the basal phalanx.

Roentgenograms showed a thickened basal phalanx of the middle finger. There was

irregular overgrowth of bone at the distal end of the phalanx and a large soft part swelling with fine calcifications

The finger was amputated and the end of the third metacarpal removed with it. Local anesthesia was used. The result was excellent.

Two weeks after amputation he returned to his work which was of a heavy manual type. He was able to use his hand without trouble. Examination on Sept 30, 1946, eight years after operation, showed a normal width of the metacarpal arch. The skin was healed, soft, and there was no evidence of tumor. Roentgenograms of the hand revealed a smoothly rounded stump of the metacarpal with no evidence of recurrence.

*Pathologic Examination* A globular subcutaneous mass distended the skin of the proximal phalanx of the third finger which had been amputated with the distal 3 cm of the third metacarpal. The mass was gray-white, rubbery and translucent on cut section, 3.5 cm long, attaining a maximum thickness of 1.5 cm. It replaced the distal centimeter of cortical bone of the dorsal surface of the phalanx and extended proximally between the periosteum and the extensor tendon almost to the metacarpophalangeal joint.

The tumor was composed of poorly encapsulated atypical hyaline cartilage in which no lobulations were seen. The cells, grouped together to form highly cellular areas, were generally ovoid or fusiform, varied greatly in size and had homogeneous acidophilic cytoplasm and relatively large round granular nuclei with conspicuous central nucleoli (Fig 1). Multinucleated cells were found in each high power field. Tumor giant cells were seen occasionally though mitotic figures were absent. Many thin-walled blood-vessels were present at the periphery of the tumor but the center was avascular and contained focal areas of necrosis.

**Case 2**—F S, No X8679, a 53-year-old tailor had mild pain in the ring finger of his left hand two years before consulting his physician. One and a half years before he had noted a swelling of the finger. He finally went to his doctor because he had steady pain in the area.

The finger was amputated in 1937.

Since the operation he has had no signs or symptoms of any kind. He returned to his work as a tailor and has worked daily since then. On Sept 27, 1946, he showed no signs of recurrence or metastasis, nine years since his operation.

*Pathologic Examination* The proximal two-thirds of this fourth finger which had been amputated at the metacarpophalangeal joint was distorted by a firm subcutaneous mass. On cut section the proximal phalanx was completely replaced by a lobulated translucent mass of refractile, milky-appearing tissue which extended along the palmar surface of the middle phalanx between the periosteum and flexor tendons. The entire tumor was 8 cm long and 4.5 cm in greatest diameter. The center of the lesion was soft and the periphery was rubbery.

Great variation in size and shape of cells characterized the atypical cartilage that formed this tumor. Most of the cells were stellate or spindle-shaped with pale cytoplasm and relatively huge hyperchromatic nuclei. Binucleate forms were moderately plentiful but multinucleated and tumor giant cells were not found. There were no mitotic figures. The thin basophilic matrix was foamy and pale. Lobules were poorly defined. The tumor was surrounded by highly vascular cellular areolar connective tissue infiltrated with lymphocytes. Tiny spicules of bone were seen near the periphery of the mass.

**Case 3**—No 161676 L L, married female, age 55, was admitted to the Strong Memorial Hospital, Feb 11, 1940. She had had mild progressive pain for one and a half years on the inner aspect of the left foot. An enlarging tumor was noted eight months ago. She had been treated for flat feet by strapping and arch supports without relief. Two weeks ago for the first time she had x-ray pictures taken. Following a biopsy she was referred to the hospital for further treatment.

Her family and past histories had no bearing on the present complaint.

*Examination* showed an obese healthy looking woman. She weighed 220 lbs. Her

vital signs were normal. She had a ventral hernia in an abdominal scar. Her left foot showed a swelling on the medial aspect at the proximal end of the first metatarsal bone. The mass was smooth, firm, not movable, and measured 5 x 7 cm. It was tender and there was edema of the tissues of the dorsum of the foot in this region. There was a limitation of subastragular motion by approximately 70 per cent.

*Laboratory studies* showed red blood cells 4,940,000, hemoglobin 14.5 Gm, white blood cells 9,600. The Wassermann reaction was negative. Roentgenograms revealed marked decalcification in all the bones of the foot. The cortical bone on the medial side of the cuneiform was partially destroyed. There was a soft tissue mass in the same area.

A mid-calf amputation was done on Feb. 13, 1940. She was discharged with a soft, well healed, non-tender stump on March 10, 1940.

She had an artificial limb fitted. This worked well till Feb. 3, 1943, when it had to be refitted. There were no signs of recurrence or metastasis at that time.



FIG 1

FIG 1—(Case 1) Chondrosarcoma of finger (x 200)

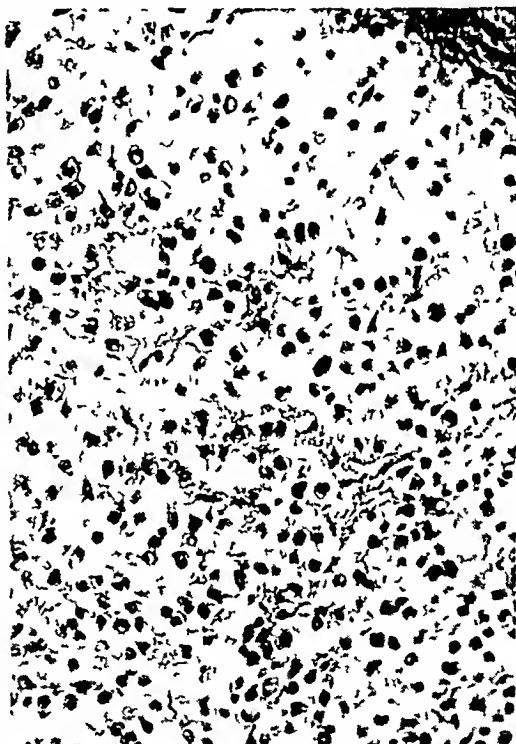


FIG 2

FIG 2—(Case 3) Chondrosarcoma of cuneiform bone (x 200)

On Dec. 30, 1946, she was working daily and had no complaints, 6¾ years since operation.

*Pathologic Examination.* A rubbery globular mass 8 cm. in diameter and 7 cm. thick protruded from the medial aspect of the first cuneiform bone overlapping the head of the first metatarsal and the navicular. On cut section the first cuneiform was almost completely replaced by soft, glistening, translucent, gray tissue continuous with the tumor extending from its medial aspect. The medial surface of the mass was covered by tough fibrous tissue but the intra-osseous part of the lesion was not encapsulated. The tumor did not encroach on the joint surfaces.

The cellular neoplasm was composed of atypical hyalin cartilage (Fig. 2). The cells were round or ovoid and varied widely in size. The nuclei were relatively large, granular

and had prominent nucleoli. Hyperchromatism was moderate. The cytoplasm was granular and acidophilic. Multinucleated cells were found in most fields but there were no tumor giant cells or mitotic figures. The matrix was generally hyalin and basophilic but some areas were foamy and stained palely. Well formed spicules of bone were seen near the edge of the tumor and its medial surface was covered by avascular collagenous tissue infiltrated with lymphocytes and plasma cells. Fibrous septa traversed the neoplasm.

**Case 4.**—V F, No 780, a 33-year-old man was admitted to Strong Memorial Hospital Dec 4, 1934.

He has had a long history of multiple fractures dating from infancy. There have been five fractures of the left femur, two of the left tibia and one of the left forearm. As a result of one femur fracture he has had a deformity of the left thigh since eight years of age. Since birth there has been bilateral dislocation of the elbows and small, hard, irregular tumors on the digits of the left hand. Soft bluish discolorations have been present on the left foot, lower leg, about the knees, left hand and forearm. In March, 1924, he had hemoptysis. He was put at bed rest for nine months. Tubercle bacilli were never demonstrated. He gained from 98 to 115 lbs during this time. There has been a right-sided nodular goitre for 11 years. For one year he has had intermittent pain in the left ankle. This pain has become steadily worse. The only relief is obtained by strapping with adhesive. He has walked with crutches since childhood and the left leg is eight inches shorter than the right. He has had occasional spells of dyspnoea, palpitation and tachycardia.

His father died at 62 of heart disease, his mother died at 69 of cancer of the rectum. One sister died at 11 of "heart trouble" and one sister died at 35 of "some blood stream disease." Two sisters are living and well. There has been no family history of bone fragility or bony deformities.

*Examination* revealed multiple deformities. There was an acne-like rash over the face, back and buttocks. The sclerae were not blue. There was an enlarged nodular goitre on the right. The heart and lungs were normal. The blood pressure was 120 systolic, 68 diastolic. The shoulder girdle, spine and pelvis appeared to be normal. The left humerus was shorter than the right with an old fracture deformity. Both radii were dislocated at the elbows. Both forearms were bowed and malformed, the left more so than the right. The left ulna showed an old fracture deformity. The fingers of the left hand have multiple chondromata as also the left toes and foot. There were many small cavernous hemangiomata on the left hand and forearm. The right leg was normal. The left leg was shorter than the right, with fracture deformity of the left femur, upper third. There was some limitation of the left hip with muscle atrophy.

*Laboratory Examinations* showed normal blood, urine and negative blood Wassermann. The blood calcium was 10.0 mgs per cent and the phosphorus 3.4 mgs per cent. Roentgenograms showed the characteristic picture of multiple cartilaginous exostoses with malformations of the bones characteristic of the disease.

He was advised to have the left leg amputated at the midthigh because it did not take part in weight bearing, was painful and a good artificial limb would allow him to discard his crutches. Amputation through the mid thigh was done under spinal anesthesia. Convalescence was without incident. He was discharged on Dec 22, 1934, in good condition. He was fitted to an artificial limb and managed it quite well. He worked hard at his concession putting in long hours daily.

Report on Dec 24, 1946, from Chicago, Ill., where he is now living was that he "is feeling fine and working daily." This is 12 years since operation.

*Pathologic Examination* The leg bones were bowed anteriorly and laterally. The skin was studded with hemangiomata, some of them pedunculated. Other hemangiomata were found in the subcutaneous tissues of the leg and foot. The bones were studded with irregular masses of typical hyalin cartilage. The second toe was almost replaced by a friable cartilaginous mass.

The lesion of the toe contained areas of atypical hyalin cartilage and others that were frankly myxomatous. These types of tissue were sometimes mixed together. The cells in the hyalin areas were moderately numerous, ovoid with relatively large granular nuclei which became hyperchromatic at the periphery of these areas. Stellate cells of the myxomatoid zones had rather small compact nuclei. Binucleate forms were found in each high power field but no tumor giant cells nor mitotic figures were recognized. The tumor was only partly encapsulated since masses of neoplastic cells were found adjacent to relatively normal appearing bone. Septa were rudimentary and vascular. Endothelial lined spaces filled with blood were found imbedded in tumor cartilage.

**Case 5**—No 150027, I L, married female, age 33, was admitted to the Strong Memorial Hospital, Feb 13, 1939. She first became aware of a hard tumor on a rib just below her left breast in April, 1933. There were no accompanying symptoms. Her physician advised watching the tumor, which was about the size of a red kidney bean. One year later it had increased to the size of a lemon. It was removed with a piece of the rib—"about four inches long" according to the patient. Convalescence was uneventful. Fifteen months later a small nodule appeared in the scar at the site of the first tumor and a second soft, non-tender, fast growing, movable, fluctuant area at the end of the scar. By the spring of 1937 she began to have aching and tenderness in the tumor. In the summer of 1937, seven irradiation treatments were given at the State Malignant Disease Institute. Tenderness and soreness increased locally following this. In October 1938 a mass was removed at a hospital in Syracuse, N. Y.

Her family and her past histories did not contribute to her present condition.

She was a well nourished, handsome young woman. Her vital signs were normal. There was a scar on the left chest from the axiphoid along the 7th rib to the axillary line. A moderately tender mass, measuring 5 x 10 cms, was present extending over the 7th, 8th and 9th ribs in the midclavicular line. There were two other movable masses of 1 x 2 cm and 1 x 1 cm noted in the anterior axillary line. The lungs were normal to physical examination. The rest of the physical examination did not reveal anything significant.

*Laboratory Studies* showed red blood cells 4,200,000, hemoglobin 13.5 Gm, white blood cells 6,000. Wassermann reaction was negative.

Roentgenograms indicated that there were no metastases in the lung fields. The tumor involved the 7th, 8th, and 9th ribs and cast a sharply defined ovoid shadow with a network of calcification within the mass.

On Feb 16, 1939, a resection of the 7th, 8th and 9th ribs was done in one block with all the intervening tissues and including the separate nodules. A good margin was given and great care taken not to expose any of the tumor. It was evident at operation that the tumor had broken through its original capsule. It had extended by direct continuity along the fascial planes and across the pleura on the inside of the chest. The diaphragm and the lung gave no evidence of involvement.

She made a good recovery and was discharged to her home on March 8, 1939.

She was completely symptom free and gained in weight until July 25, 1939. Then she had pain starting in the mid-dorsal spine and radiating around the chest wall along the scar. Pain was accentuated by motion, standing, fatigue, and relieved by recumbency. The pain had become persistent and severe so that she had been given "pain pills" for relief.

On examination she showed tenderness over the 6th dorsal vertebra and moderate sensitiveness in the scar. There were no evidences of recurrence at the site of operation. Nothing else of importance was found. Studies on the blood were almost identical with those of her first admission.

Roentgenograms showed malignant invasion with destruction of the left pedicle of D6, both pedicles of D7 and a partial involvement of the posterior aspects of the bodies of both D6 and D7. There was moderate deformity of the paravertebral structures. Radiation treatment with x-rays was given consisting in 2000 "r" units in 10 days. She was



## CHONDROSARCOMA

placed on bed boards and at complete bed rest. Relief from the pain was quite marked as long as she was recumbent. Upon getting up pain returned with lessened severity. She was discharged on Oct. 21, 1939.

In late December, 1939, her right leg became weak and slightly numb. In another month both right and left legs had become completely paralyzed with loss of all sensation. There was also incontinence of urine and feces. On this admission there was a kyphosis at D7-8 and 9, complete loss of sensation below D8, a small nodule on the left third rib in the mid-clavicular line, and a freely movable lemon-sized mass above and lateral to her right breast. Her hemoglobin was now 12.2 Gm. Stereo examination of the spine indicated marked destruction of the bodies of the 6th and 7th dorsal vertebrae and involvement of the rib ends. There was also invasion of the 11th rib and the 11th dorsal vertebra. Gallstones were present. She responded well to aspirin and codeine therapy. She was put on constant bladder drainage. She was discharged to her home on June 29, 1940, where she died during the summer.



FIG. 3—(Case 5) Recurrent chondrosarcoma of rib

*Pathologic Examination*—The specimen, weighing 250 Gm, consisted of segments of three ribs, each 14 cm long. The central rib was obscured by a resilient circumscribed ovoid mass measuring 9.5 x 6.5 x 6 cm which covered the central part of the adjacent ribs and distorted the pleural and muscular surfaces of the specimen. Mucoïd material oozed from the gray translucent lobulated cut surfaces leaving scattered craters lined with ragged tissue. The central rib was entirely destroyed within the tumor and the adjacent ribs were eroded. A tongue of nodular tumor tissue extended dorsad along the outer border of the central rib invading the intercostal muscles. A rim of normal appearing bone and muscle at least 1 cm wide separated the tumor from the dorsal edge of the specimen (Fig. 3).

The cartilage in this neoplasm was atypical and highly cellular. There were ovoid cells with relatively large vesicular nuclei and spindle-shaped and stellate cells with relatively small hyperchromatic nuclei. These types were present in approximately equal concentrations. Cytoplasm was scanty. Binucleate forms were commonly found but no tumor giant cells or mitotic figures were seen. The matrix was pale and vacuolated and was absent in the areas where the stellate and fusiform cells predominated. The tumor was confined by a thin rim of poorly vascular collagenous tissue.

The nodules noted in the intercostal muscles possessed the same cytologic characteristics as the parent tumor. They were circumscribed but not encapsulated.

**Case 6.**—M. F., No. 104576, a 54-year-old housewife, was admitted to Strong Memorial Hospital on July 15, 1935.



She suffered a severe fall injuring her right thigh and knee eight years ago. While on ship board three years ago she had another fall. One year ago she noticed difficulty in getting up and down stairs. She began to have stabbing pains radiating around her left chest from the spine to the lower portion of the sternum three months ago. For several weeks while this pain persisted there was an extremely sensitive zone in the involved skin area. For the first time one month ago she had numbness of her feet. This numbness has gradually progressed upward with a sense of weakness at the same time. She has had to use crutches to get around.

Her family and past histories were non-contributory.

*Examination* gave tenderness on pressure over Th 3, 4, and 5. There were hyperactive biceps and triceps reflexes on the left, and a bilateral positive Babinski. Sensory changes to pin prick, touch, hot and cold at Th 6. Vibratory sense was lost below level of ischial spines.

*Laboratory studies* showed normal blood and urine. Wassermann on the blood was negative. Radiograms showed a destructive erosion of the pedicles of Th 4 compatible with tumor growth.

Laminectomy was done. A hard, round, circumscribed nodular tumor was encountered. It measured 3.5 x 4.0 cm in diameter. There were two portions of the growth, one involving the muscles of the back and the other an intraspinal extension. All the tumor was looped out except for a thin shell which was left between the 4th and 5th ribs on the pleura.

The postoperative course was uncomplicated. The positive Babinski bilateral signs disappeared. She had almost complete restoration of the power of her lower extremities. She was discharged on Aug 5, 1935.

She was readmitted on July 28, 1936. She had regained full use of her legs and her only complaint was crampy pains over the left scapula. These pains first appeared in Mar 1936 and had gradually increased in severity, causing her to cry out. There had been sweating of the right side of the face, right arm and axilla for the past three weeks.

On examination the only significant finding was that the right knee jerk was a little more active than the left.

Laminectomy with partial excision of the tumor was carried out. The tumor had extended into the thoracic cavity.

She was discharged in good condition on Aug 18, 1936.

Her third admission was on June 8, 1937. At this time she had difficulty in walking and pain in the right hip. She had a band of anesthesia corresponding to T3 and T4 (two roots sectioned at last operation). The right leg was weaker than the left. Roentgenograms showed traumatic arthritis right hip—old (injury).

Her fourth admission was on Jan 3, 1938, because of inability to walk. This complaint had been present one week. There was discomfort, weakness and pain in the right shoulder and in both thighs. There was anesthesia to pin prick, touch and temperature to Th 2. The old incision was opened and access to the intrathoracic portion of the tumor was obtained by removal of portions of 3rd, 4th and 5th ribs. Tumor tissue was resected as completely as possible. She made a beautiful recovery with return of sensation to practically normal. A course of deep roentgenotherapy was given.

She died at her home in the summer of 1939. No postmortem study was made.

*Pathologic Examination* The three surgical specimens appeared similar. They were moderately small pieces of cartilaginous tissue varying in consistency from soft to firm.

The original neoplasm was made up of atypical adult type hyaline cartilage in which groups of small ovoid cells were separated by homogeneous basophilic ground substance. The cells had acidophilic cytoplasm and relatively large granular nuclei. Multinucleated forms were seen in each high power field but there were no tumor giant cells nor mitotic figures. Some areas were necrotic. A moderately vascular capsule was seen in some areas.

but tumor cells filled the marrow spaces of adjacent bone. Septa were poorly defined (Fig 4).

The first recurrence was more cellular. Nuclear hyperchromatism was conspicuous. Some bizarre nuclei were seen. The entire lesion was more vascular than the original tumor (Fig 5).

The second recurrence was more anaplastic although still recognizable as chondroid tissue. The hyalin matrix contained acidophilic fibrils. Tumor cells were larger and giant forms were found easily but only a few mitotic figures could be seen. The periphery of the neoplasm was very vascular (Fig 6).



FIG 4

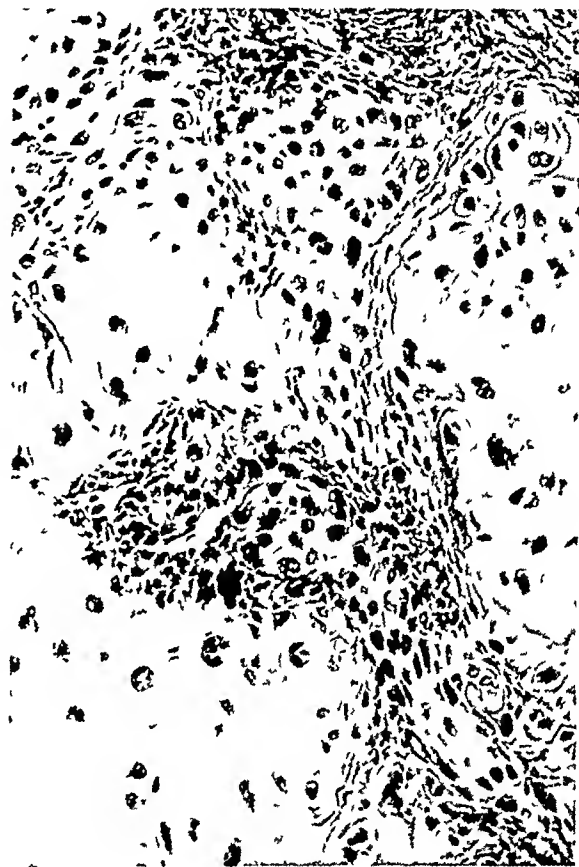


FIG 5

FIG 4—(Case 6) Chondrosarcoma of spine. Photomicrograph of original tumor ( $\times 200$ )

FIG 5—(Case 6) Recurrent chondrosarcoma of spine. The tumor is more poorly differentiated than the original neoplasm excised one year previously ( $\times 200$ )

Case 7.—Hosp No 90595, H A, single female, social service worker, age 40, was admitted to the Strong Memorial Hospital, June 22, 1934. While looking in a mirror three months previously she had noticed that the left hip was more prominent than the right. On examining the hip she had found a tumor. Two months ago she had had pain down the lateral and posterior surfaces of the left leg as far as the ankle. This pain was worse when she worked hard or got tired. It was worse at night and had persisted till the time of admission. There had been tenderness over the swelling recently but no motor weakness. She had been dieting and had lost 18 pounds.

In June, 1933, she had a sudden attack of blindness in the left eye. She went to an ophthalmologist who diagnosed a thrombosis of the central artery of the retina. Under his treatment she had recovered part of her vision in the lower half of the field but the upper half remained blind.

She had had bilateral slipping patellas since childhood. One side had been dislocated 13 times, the other 14 or 15 times. Her father, a physician, had always reduced the dislocations without difficulty. There had been no slipping in the last 10 years.

She was well developed and obese, comfortable and cooperative. There were many pin-head to bean-sized rusty areas of keratosis over the trunk. The vision was normal in the right but only 20/200 in the left eye. The left pupil was slightly larger than the right. The left fundus showed secondary optic atrophy with marked reduction in the calibre of the retinal arteries. There was a huge swelling in the left gluteal region extending as low as the gluteal fold. It distorted the whole gluteal area. The tumor extended almost to the midline of the abdomen, above the iliac crest and down to the level of the left greater trochanter. It was deep under the muscles, was firm, semi-clastic. There were a few dilated vessels in the skin over it and a sensation of increased warmth. No nodes were palpable in the groin. Rectal examination gave no evidence of extension into the pelvis. The tumor area measured 150 cm x 80 cm x 80 cm. There was no limitation of motion in the femur.

*Laboratory Studies* showed red blood cells 5,600,000, hemoglobin 13 Gm, white blood cells 6,400. Wassermann on the blood was negative. Roentgenograms of the chest were negative for metastases. Roentgenograms of the left pelvis showed multiple patches of partial calcification scattered over the region of the buttocks. There were three distinct punched out areas through the upper portion of the ilium as if invasion had taken place. The roentgenographic picture was typical for chondrosarcoma of the ilium.

The consensus was that operation could not be done and although this type of tumor was known to be radioresistant, a course of radiation therapy was decided upon. During the next six months she received x-radiation therapy in 300 r doses for a total of 13,500 r. There was no appreciable effect upon the tumor. Accordingly on Jan 3, 1935, the tumor was exposed and found to spring from a 10 cm wide base near the upper crest of the ilium. This pedicle was divided with a chisel and the main portion of the tumor thus removed. The area of the pedicle was next chiseled out with a good margin, making a hole through the bone. Several small fragments of cartilage were broken off during the operation and the wound was thoroughly washed out at the close. The gluteus muscles were preserved carefully. Silk was used throughout. The operation took three hours. There was no shock. A transfusion of 400 cc of citrated blood was given late in the day. The wound healed by first intention. She was discharged on the 11th postoperative day. She recovered rapidly, walked without a limp and resumed her job as a visiting social service worker a month after operation. Roentgenograms showed a hole through the ilium and no signs of remaining tumor in the bone.

Six months later (June 19, 1936) a good sized nodule was found in the scar. It was removed without ever exposing any of it.

Her next recurrence was discovered on Oct 29, 1937. It was excised with the radio-knife without any difficulty.

In Nov of 1938 she began to get sciatic pain along the back of the left thigh. She walked with more of a limp. No signs of recurrence could be found on examination. By Jan 1940 it became apparent that she had another tumor. On Mar 11, 1940, the tumor was again excised. It arose from inside the ilium and had extended through the opening made in this bone. It was very difficult to dislodge and finally in order to control bleeding from the sciatic artery, it was necessary to remove it rapidly in pieces. The tumor consisted of firm cartilage. It weighed 1270 Gm and measured 180 x 150 x 100 cm. Sero-sanguinous fluid collected in the dead space necessitating aspiration. She went home in good condition on the 12th postoperative day.

In Dec of 1940 she presented two recurrences—one the size of a hen's egg—the other, the size of a ripe olive. These tumors were easily removed. They measured 70 x 50 x 40 cm, and 20 x 20 x 40 cm respectively. She was in the hospital for 11 days. She continued to have sacro-iliac and sciatic tenderness and numbness in the great toe. Local injections with 1 per cent procaine and epidural injections of 0.5 per cent procaine

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produced temporary relief. Physiotherapy was of some help but the pain became so persistent that a chordotomy was performed at the level of D4-5- and 6. She was completely relieved of her pain by this procedure and was discharged on June 22, 1941.

Her next admission was in July 1941. A large trilobed tumor with an intrapelvic extension and two posterior ones was removed. The sciatic nerve had been compressed to a thin area by the pelvic portion of the tumor. The tumor measured 10.0 x 10.0 cm, weighed 500 Gm. It was cystic in the interior containing a thick tapioca-like gelatinous material. She was discharged on the 16th day after operation. There was a foot drop and flail-like ankle. A foot drop brace was necessary to stabilize her walking.

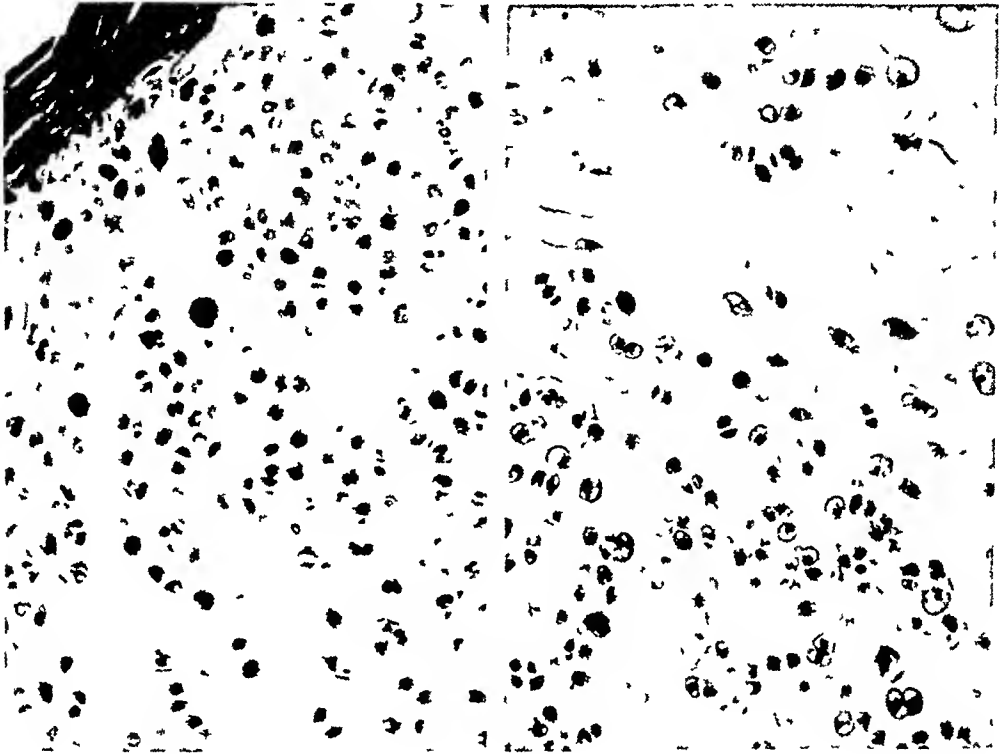


FIG 6

FIG 7

FIG 6—(Case 6) Second recurrence of chondrosarcoma of spine. Case 6 more anaplastic than previously excised specimens (x 200).

FIG 7—(Case 7) Chondrosarcoma of ilium. Photomicrograph of original tumor (x 200).

It was necessary to aspirate fluid from the dead space left by operation. This was done about once a month for the next three months. She worked daily making up to 10 calls on some days. In late October 1941 culture of this fluid showed non-hemolytic streptococci and *S. albus*. The area was incised and drained. Gramicidin was introduced into the abscess cavity. It healed in about one month but in Mar. 1942 the tumor had extended through the scar ulcerating the epithelium over it. Consequently on Apr. 2, 1942, this nodule was excised and she went home two days later. She continued with her work coming to the office for dressings. The wound was infected with *Staphylococcus aureus* and *B. proteus*. It had a disagreeable odor which was cleared by treatment with azochloramide in triacetin oil. Dressings were done every two or three days with slow healing but tumor tissue began to appear again. Accordingly the whole area was curetted out under sodium pentothal anesthesia on June 12, 1942. Gramicidin was introduced into the cavity and alternated with acetic acid 0.5 per cent as *B. pyocyaneus* infection as well as *B. proteus*.

was present. The situation appeared to be very bad but healthy granulations formed and pinch grafts were applied to them. She was discharged on July 26th. For the remainder of the year she continued with her work although the wound required much attention. She also developed lack of bladder control and frequency. She also had progressive constipation. It was found that she had loss of vesical and anal sphincter tone on a neurological basis. She had acute pyelitis and cystitis due to *B. coli*. Sulphadiazine brought the temperature to normal and gave relief to her bladder symptoms.

On Mar 7, 1943, she was admitted to the hospital for the last time. She had had six weeks of gradually progressive intestinal obstruction. Her bowel movements had decreased



FIG 8—(Case 7) Macroscopic appearance of typical recurrent chondrosarcoma

to two times a week. She had had loss of appetite, nausea and vomiting increasing in frequency. The tumor had grown rapidly in size. She had lost weight. Everyone was much impressed by her courage in facing her problem. There was a firm irregular mass in the LLQ inguinal area. There were huge firm fixed nodules over the left hip and iliac area. Her course was progressively downhill. She had a chill with cyanosis and dyspnea on Mar 12th, possibly a lung metastasis. On the 17th her left leg became tremendously swollen and edematous. She became moribund on the 19th and expired quietly on March 22, 1943.

*Pathologic Examination*—The globular, coarsely nodular, firm, original specimen weighed 1,415 Gm and measured 19 x 13 x 11 cm. It was enclosed in a tough fibrous capsule which was continuous with the periosteum of the bony pedicle by which the lesion was attached to the ilium. The cut surfaces were made up of a mosaic of firm, translucent, gray hyalin cartilage, softer areas of gelatinous consistency and stony hard foci of yellow-white gritty material. Well formed fibrous septa traversed the mass. The base of the tumor was sharply delimited from the bony pedicle but the adjacent bone appeared eburneous.

Histologically the neoplasm was composed of atypical hyalin cartilage which was well encapsulated and lobulated but poorly vascular. All of the cells were ovoid, lay in lacunae, and had well defined acidophilic cytoplasm with small compact nuclei. Sections taken from the periphery of the tumor were more cellular and the nuclei were relatively much larger. Binucleate forms were found only in these regions. Spotty areas of calcification were found throughout the mass (Fig 7).

All of the recurrences appeared similar on macroscopic examination. They were generally spherical or ovoid and rubbery. All were encapsulated and on cut section mucoid material filled with irregular masses of soft cartilage escaped from the centers. This gave the lesions the appearance of thick-walled cysts with extremely ragged linings. The walls were translucent, gray-white and firm (Fig 8).

Each of the first four recurrences had a similar histologic pattern resembling, in general, the peripheral part of the parent tumor. The cartilage, though distinctly hyalin in type, was moderately cellular. The cells were ovoid, small and possessed relatively large nuclei. Their cytoplasm was coarsely granular. Lobulations were indistinct and the rudimentary septa were highly vascular.

The fifth recurrence was different from any of the previous material examined from this patient. It was far less cellular but the cells had relatively huge nuclei. Many cells were round and had several nuclei arranged peripherally in the cytoplasm forming crescentic structures.

The sixth recurrence resembled the original tumor.

There was no difficulty in recognizing the tissue from the seventh recurrence as cartilage but it was the most anaplastic of all the specimens. The round cells varied widely in size. Their nuclei were relatively enormous and cytoplasm was granular in small cells, vacuolated in the larger ones. Multinucleated forms were plentiful. The matrix was hyalin in some areas, foamy in others but lacunae were generally well defined. The few fibrous septa that penetrated the mass were extremely vascular and some endothelial lined spaces filled with blood were found imbedded in cartilage (Fig 9).

The specimen obtained at postmortem examination contained all of the types of tumor described above excepting that of the seventh recurrence. The capsule was deficient. Tumor cells infiltrated the surrounding tissues. Binucleate cells were commonly seen and most nuclei were relatively large. No metastases were found.

**Case 8—C C, No 2707,** a 21-year-old girl was admitted to the Strong Memorial Hospital Sept 4, 1926.

She was suffering with severe sacroiliac pain, urinary incontinence, extreme constipation and vomiting. She had had a sudden attack of severe pain in the left sacroiliac region 20 months ago. She was in bed for one month before the pain left. A swelling in the sacral region with some tenderness was discovered and there was "black and blue" skin discoloration of the perineum at this same time. Early in the attack she had loose watery stools but within a short time constipation was the rule. She had passed mucus and blood in the stools. She returned to her work after one month and worked until 13 months ago. Then the attack was repeated. After five days an exploratory operation was done and an inoperable sarcoma was found. She had to be catheterized four times while in the hospital. Eight months ago pain recurred again and the swelling became more pronounced. She was given a course of roentgen ray therapy. Pain disappeared for three months but upon its return another operation of some sort was done. The pain increased in severity requiring morphine for relief. Loss of appetite and vomiting became the rule. She dropped 16 pounds in weight.

Her family history had no bearing on this condition and she had always been healthy herself until this illness.

Examination revealed an emaciated girl, sallow in complexion and in much pain. The abdomen showed a prominent bulging on the right from the umbilicus to the pubis. A

tumor was readily palpable, arising from a hard firmly-fixed posterior growth. Two scars of previous operations were present in the midline. The vulva were gaping and the perineum bulging from the pressure of a hard firmly attached smooth tumor which filled most of the pelvis. She was totally incontinent of urine. A mass could be palpated by rectum. There was a visible tender swelling over the right sacrum.

*Laboratory studies* gave RBC 5,110,000, hemoglobin 80 per cent, W B C 5,000. Wassermann on the blood negative. Roentgenograms showed a tumor mass completely obliterating the lower part of the sacrum. There were strands of calcification in part of the tumor.

Because of intestinal obstruction a colostomy was done on Sept 11, 1926. This relieved her obstructive symptoms and the bowel functioned well through the artificial opening for two months until she succumbed.

*Pathologic Examination*—Tissue removed from the pelvic mass at operation was made up of partly encapsulated, avascular, poorly formed chondroid tissue. The cells varied widely in size and shape with blunt spindle and ovoid cells predominating. The large granular nuclei had prominent nucleoli. The matrix was foamy, basophilic, mucoid material. No lacunae were present. Tumor giant cells and mitotic figures were not found.

At postmortem examination a tumor mass at least 20 cm in greatest dimension projected from the ventral surface of the sacrum, which was almost completely destroyed. The mass extended into the recto-vaginal septum, through both sacro-sciatic notches and destroyed both sacro-iliac joints and the adjacent portions of the ilia. On cut section the mass contained many cysts filled with a mixture of gelatinous material and friable pink gray tissue which made up the bulk of solid material in the neoplasm. The estimated weight of the tumor was 2,500 Gm. Metastases were found in the superior ramus of the left pubis and implants of polypoid, cystic tumor nodules were seen throughout the peritoneal cavity. The tumor produced bilateral hydronephrosis and obstructed the sigmoid colon.

Sections from the tumor and its metastases appeared identical with those examined from the surgical specimen (Fig 10).

**Case 9**—No 137039, L. L., single female, age 60, was admitted to the Strong Memorial Hospital, Nov 21, 1937. On Mar 18, 1927 a tumor of the right chest wall was removed in Ogdensburg, N. Y. Portions of the 3rd and 4th ribs were taken with the hard nodular tumor which was reported from the Bender Albany laboratory as benign chondroma. She had had it about five years before operation. There had been no recurrence. Three years ago (1934) she discovered a small swelling in the right lumbar region. It gave no symptoms till one year later. For the last two years there had been a stinging and burning sensation in this region especially when she became tired. Two months ago the discomfort increased in severity and there was radiation down the anterior aspect of the right thigh. The swelling grew rapidly in size. Medication was necessary to relieve pain and to permit sleep.

She had an injury to her back five years ago. It caused soreness for several days but there had been no subsequent symptoms. For 2-3 years there had been attacks of dizziness, coming on suddenly and lasting several days.

She was a well developed, well nourished woman with arteriosclerotic vessels. There was an operative scar under the right breast with a defect in the bony cage due to removal of the 3rd and 4th ribs. In the right lower back was a large firm mass occupying the position of the posterior right ilium. It extended as far up as the rib cage on the right and as far over as the sacro-iliac joint which was partially obscured by it. It had a bony firmness. There were many dilated skin vessels over it and a locally increased temperature. There was no pulsation in the tumor. Movements of the lumbar spine were definitely restricted. The mass measured 10 x 15 cms in diameter.

*Laboratory studies* showed red blood cells 4,160,000, hemoglobin 12.5 Gm, white blood cells 6,300. Her blood pressure was 145 systolic/90 diastolic. There were 15-20

white blood cells and 1-2 red blood cells per high power field in the urine. Blood calcium was 9.4 mgs per cent, blood phosphorus 4.2 mgs per cent, serum albumin 3.16 Gm per cent, serum globulin 2.0 Gm per cent. Roentgenograms showed a massive bone tumor of the right ilium which replaced all the normal bone adjacent to the right sacro-iliac joint. The bone had a cystic appearance with ill defined septa, typical of chondrosarcoma.

A partial resection of this large tumor was carried out on Dec 7, 1937. It was impossible to remove the portion which extended across the region of the sacro-iliac joint. Tumor tissue was curetted away to bare bone wherever feasible. There was considerable loss of blood. The wound became infected with *S. aureus* and for one week she ran a fever. Roentgenograms of the chest showed a resected area of the 3rd and 4th anterior ribs and a metastatic nodule 4 cms in diameter near the right costophrenic angle. She was discharged feeling quite well with relief of pain 30 days after operation. The wound was still draining somewhat.

*The nodule in the lung field was considered a long standing one as it showed a large size and dense structure.*

Following operation she gained in weight and strength. She had little trouble in getting around. Only occasionally did she have a twinge in her thigh. She was seen in Oct 1939, had been to the World's Fair in New York without any difficulties. She came for check up as she was having dizzy spells and some return of the pain in her right sciatic distribution. Her brother, a physician who referred her here, had died of coronary heart disease five months before, leaving her without family connections. She feared that she would become a chronic invalid and was tense and apprehensive. On this examination she showed an increasing hypertension with blood pressure of 180/96—a slightly enlarged heart. Films of the chest showed a slight increase in the size of the lesion—it now measured 5 cms as compared to 4.2 cms in 1937. There was a local recurrence in the pelvis but it appeared that the partial removal of the tumor had been worthwhile.

She came into the hospital for the third time on June 26, 1940, because of pain in the right hip. This pain was worse in walking. It radiated down to the calf. Examination showed some extension of the bony tumor lateralwards but not marked. Her hypertensive symptoms were uncontrolled. She still had dizzy spells and nausea. A course of radiation 1,400 r units gave only partial relief from her pain.

At her fourth admission on January 9, 1941, she stated that she had had considerable relief from her x-ray therapy of six months ago. Also, the hypertension symptoms had been much improved. There was a hard mass in the right ilium—15 cms in diameter. The red blood count was 4,730,000, hemoglobin 15 Gm and white blood count 5,600. Roentgenograms showed no change in the bone tumor but a slight increase in the metastatic tumor in the right lower lung field. It now measured 6 cms across. Radiation treatment with 2,100 r units gave some but not complete relief.

Her fifth and last admission was for severe pain in the epigastrium with radiation to the back between the scapulae. It had begun three days previously. There was nausea but no vomiting and bowel movements had been regular. The pain shifted to the paraumbilical region especially to the right. Her temperature was 38.5°, pulse 96. Respirations 24, blood pressure 190 systolic/85 diastolic. There was marked generalized abdominal spasm and tenderness over the region of the gallbladder. The white blood count was 12,000. She was watched and showed improvement, the tenderness subsiding in three days. There had been persistent distention despite treatment. Paracentesis showed no fluid. Roentgenograms revealed a distention of the small bowel consistent with obstruction. At operation under pentothal sodium and local procaine the gallbladder was normal. A left ovarian cyst was impacted in the pelvis, trapping the small intestine. The cyst was easily removed freeing the bowel. Closure was made with silk. Although the operation was simple and practically without blood loss, the blood pressure dropped rapidly during operation following administration of the sodium pentothal. She was given plasma with a restoration of her pressure to normal. But during the night her condition became worse. Her temperature rose to 41°, the pulse was rapid and weak. The next day her fever



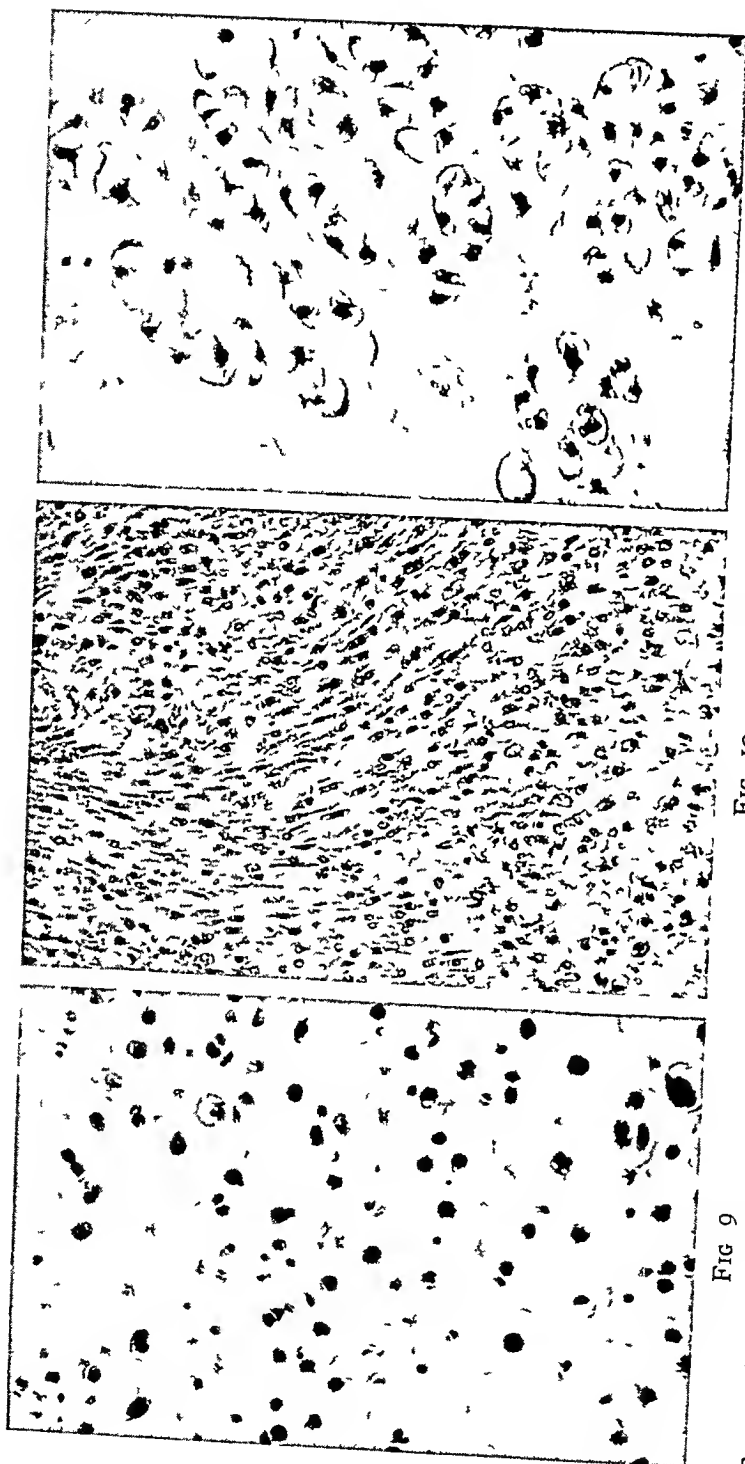


FIG 9

FIG 10

FIG 11

FIG 9—(Case 7) Recurrent chondrosarcoma of ilium original operation Note greatly increased size of nuclei ( $\times 200$ )

FIG 10—(Case 8) Chondrosarcoma of sacrum Note absence of lacunar cells and myxomatous appearance Case 8 ( $\times 200$ )

FIG 11—(Case 9) Chondrosarcoma of ilium Little is seen to suggest a malignant neoplasm yet local recurrence and pulmonary lesions appeared no more anaplastic Photomicrograph Case 9 ( $\times 200$ )

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remained elevated, the blood pressure fell off gradually Examination showed spasticity of the extremities and bilateral positive Babinski reflexes She did not rally and expired on July 2, 1941

*Pathologic Examination*—The specimen consisted of numerous irregular pieces of friable, pink-gray cartilaginous tissue having a combined weight of 955 Gm Some of the larger masses contained crateriform spaces with ragged walls

Histologic examination revealed moderately atypical cellular hyalin cartilage with abundant basophilic matrix Lobulations were distinct Stellate and fusiform cells with small compact nuclei predominated at lobular peripheries but ovoid lacunar cells were found in the more central portions The ovoid cells had vacuolated cytoplasm Some of

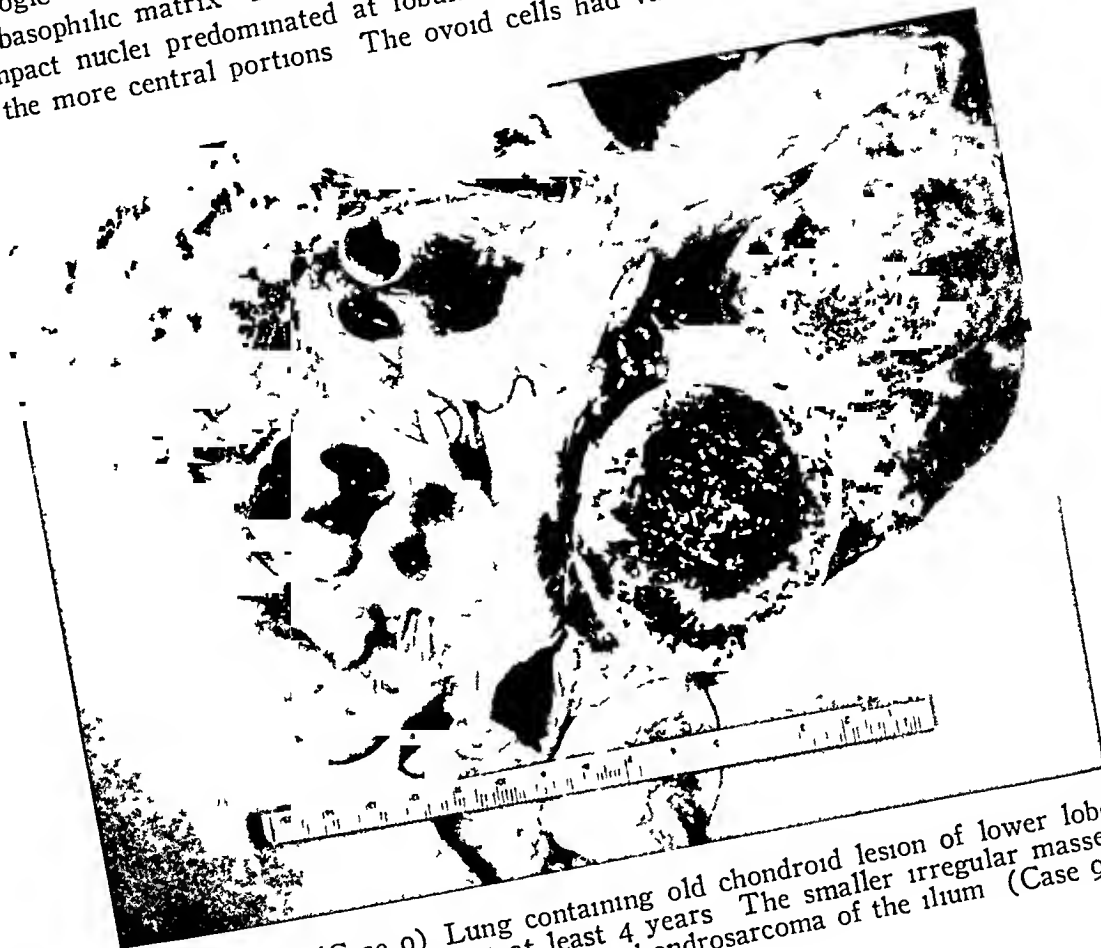


FIG 12—(Case 9) Lung containing old chondroid lesion of lower lobe known to have been present at least 4 years The smaller irregular masses probably represent metastases from a chondrosarcoma of the ilium (Case 9)

them approached "signet ring" types with a large central vacuole surrounded by a thin rim of cytoplasm containing a flattened nucleus The other ovoid cells had small round or ovoid granular nuclei with one to three distinct nucleoli Only a few relatively large nuclei could be found and there were no binucleate cells, tumor giant cells or mitotic figures Some of the pieces appeared to be definitely encapsulated by moderately vascular connective tissue which contained a few tiny well formed spicules of bone (Fig 11)

At postmortem examination a large mass of soft, friable cartilaginous tissue replaced much of the posterior portion of the right iliac bone The mass contained cysts with ragged walls from which yellow, serous fluid escaped An encapsulated red-brown, fluctuant mass 6 cm in diameter lay near the medial aspect of the base of the right lower pulmonary lobe Clear amber syrupy fluid escaped when the mass was cut leaving a firm ragged dark red wall 4 mm thick in which focal areas of gristle could be seen A second circumscribed mass 4 cm in diameter lay in the posterior portion of the middle lobe of the right lung It was firm and its cut surfaces were pearly white with a central area of green-red necrotic material Two other pulmonary masses of similar character, each 2 cm

in diameter, were found nearby. No connection with bronchi could be demonstrated in any of the pulmonary lesions (Fig 12).

The pelvic mass was distinctly more cellular than formerly and the matrix, while essentially hyaline, appeared stringy and foamy. Lacunae were well formed. Most of the cells were ovoid with small dark nuclei but a few stellate and spindle-shaped cells were found in lobular peripheries.

Tissue from all of the pulmonary masses appeared similar histologically. They were completely encapsulated masses of atypical adult type hyaline cartilage. The cells varied in size but all were ovoid with small dark nuclei and lay in lacunae. The matrix was well formed. The largest mass was partly calcified.

Another pertinent finding at necropsy was bilateral massive adrenal hemorrhage.

**Case 10**—No 248107, W. S., widower, age 46, was admitted to the Rochester Municipal Hospital, May 17, 1946. He was in good health till seven weeks ago. At that time he had a sharp pain in his right lower thigh. The pain lasted for a short time and recurred about two weeks later. He found a mass the size of his fist on the iliac bone. One week ago he had a pulling sensation in his right testicle and a dull aching pain in his right thigh. He consulted his doctor who took x-rays and referred him to this hospital. He had lost eight pounds in a year but did not know when.

In his past history he had been healthy. He had had no disease of any sort. His family history had no bearing on the present illness.

Examination revealed a well developed and well nourished man. He was in need of some dental care for cavities. He had a blood pressure of 180 systolic/100 diastolic. There was a bony hard mass in the right lower quadrant fixed to the crest of the right ilium. It measured 15 cms. in diameter and was smooth, rounded and slightly tender. The external border of the ilium was thickened but the major part of the tumor extended medially and posteriorly toward the sacro-iliac joint.

*Laboratory studies* showed red blood cells 5,210,000, white blood cells 7,000, hemoglobin 16 Gm. The platelets and the differential count were normal. The Wassermann reaction was negative. His blood contained calcium 10.2 mgs. per cent, phosphorus 4.0 mgs. per cent, acid phosphatase 2.1 and alkaline phosphatase 5.9 King-Armstrong units. Roentgenograms of the chest were negative for metastases. The right ilium in its posterior portion contained a tumor mass which measured 9.0 x 10.0 cms. This consisted of clear zones surrounded by patchy dense calcified areas, irregular in outline and ragged in appearance. It was a typical chondrosarcoma. The lesion extended almost to the transverse process of the 5th lumbar vertebra.

On May 22, 1946, a wedge of ilium was taken out giving a good margin to the tumor all around it. It was necessary to remove the transverse process of the fifth lumbar vertebra in order to get access to the tumor. A bridge of bone was preserved from the sacro-sciatic notch to the sacrum. The peritoneum was not entered but pushed aside to expose the growth. The tumor had extended posteriorly under the gluteus muscle. The muscle bundles were divided down to the bone which was exposed all the way to the sciatic notch. Closure was made in layers with silk. The operation took three hours. Ether anesthesia was used. Transfusion of 1,500 cc. of blood and 700 cc. of normal saline was employed throughout the operation. There was no shock. He had retention of urine postoperatively. It was necessary to put him on constant drainage. Sulfadiazine was given. He developed a wound infection and an abscess in the dead space. This was drained. *B. subtilis* was cultured from the pus. His wound was treated by hot compresses and he was given penicillin. The wound granulated and slowly healed. He was discharged on July 15, 1946, to get about on crutches. On Aug 5, 1946, he was in excellent shape. He had an aching sensation on sitting but no pain elsewhere. He had not borne weight but roentgenograms taken as check films postoperatively showed a surprisingly good bridge of bone which appeared to be substantial enough to stand stress.

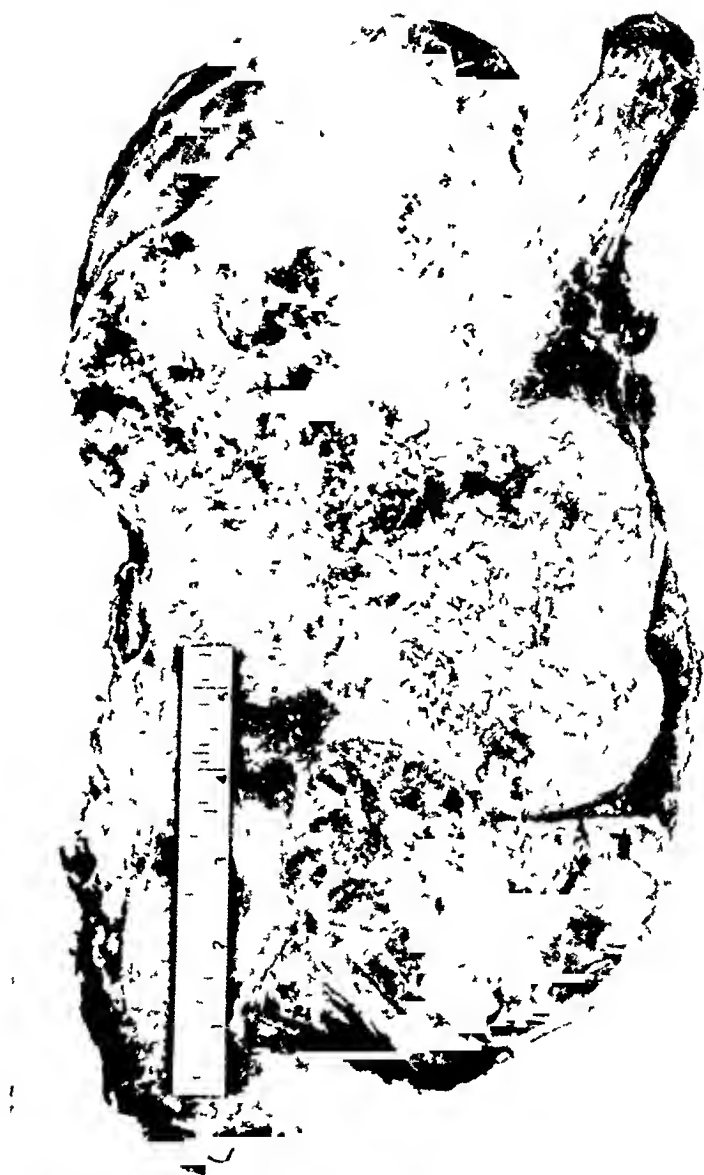


FIG 13—(Case 10) Chondrosarcoma of ilium, posterior view Case 10

He was readmitted on Nov 6, 1946. He had gained 30 pounds since his previous admission. There had been pain in the course of his sciatic for about one month. A mass, which felt hot, was noted near the anterior superior spine about one week previously. It was excised with a wide margin and a portion of the ilium taken with it on Nov 11, 1946. Following this operation he suffered with sciatic pain and numbness and tingling over the plantar surface of the foot. A myelogram showed a space displacing mass at the 5th lumbar disc space. This area was explored on Dec 23, 1946, and a metastatic nodule was found. Bilateral chordotomy was done under local anesthesia at the level of 3-4 and 5th thoracic vertebrae on Jan 8, 1947. This gave him freedom from pain. He had incontinence of bowels and bladder for some weeks after operation. The bowels gradually improved but it was necessary to do a suprapubic cystostomy on Feb 27, 1947. Paraplegia developed gradually and a mass appeared in the right lower quadrant of the abdomen. Exitus occurred June 12, 1947.

*Pathologic Examination*—The original specimen consisted of the posterior two-thirds of the right ilium including the sacro-iliac joint and a strip of sacrum 15 cm wide. Globular firm masses protruded from the medial and lateral surface of the ilium. On frontal section the central third of the bone was replaced by a firm, gray mass which spread beyond the bone conforming to the outline noted on external examination. The entire tumor measured 15 x 10 x 8 cm. It was circumscribed but not encapsulated. The superior and inferior thirds of the mass were gray, translucent, lobulated and firm, obviously cartilaginous. A cystic space 3 cm in diameter filled with partly clotted blood was seen at the superior pole and the tissue about this area was yellow-gray and soft. The middle third of the neoplasm was less cartilaginous containing irregular areas of opaque, yellow-gray gritty material. The ilium adjacent to the lesion was eburnated (Fig 13).

On histologic examination the major part of the tumor was composed of atypical adult type hyaline cartilage with well defined lacunae and basophilic homogeneous matrix. The cells were generally small but varied widely in shape. Nuclei were small and compact. No tumor giant cells or mitotic figures were found. Binucleate cells were seen rarely. Areas of necrosis and calcification were found in many sections. Myxomatous foci were encountered infrequently (Fig 14).

An entirely different picture was seen in sections taken from the periphery of the middle third of the neoplasm where numerous spindle-shaped cells of variable size formed a network about endothelial-lined blood spaces. This tissue invaded bone and adjacent soft parts. Several small foci of similar appearance were found in sections taken from widely scattered areas leading one to believe that this type of reaction may have been multicentric in origin.

A third type of tissue, more anaplastic than the others, was found about the blood-filled cyst where closely packed spindle-shaped cells formed a poorly fasciculated mass. There was marked variation in nuclear size and shape. Hyperchromatism was pronounced. Mitotic figures and tumor giant cells were seen. Collagen was present in small quantities. The edges of this tissue lay next to atypical hyaline cartilage but there was no evidence of a transitional pattern between the two (Fig 15).

The soft parts about the tumor were generally atrophic and infiltrated with lymphocytes. No real capsule could be found. Skeletal muscle was infiltrated by typical tumor-cartilage in some regions.

The first recurrence excised from this patient was received in the laboratory as a piece of the right ilium measuring 4 x 4 cm to which were attached skin and subcutaneous tissue. A hard spherical mass 4 cm in diameter lay next to the lateral aspect of the bone. The cut surface of the tumor was gray marked with areas of hemorrhage and cyst formation. A circumscribed stony hard nodule 1 cm in diameter lay in the subcutaneous tissue about 1 cm from the larger mass. This had a red-gray cut surface.

Tissue from the larger mass contained interlacing bundles of spindle-shaped cells which varied markedly in size. Collagen was plentiful. The smaller mass contained only

# CHONDROSARCOMA

poorly outlined ovoid cells with homogeneous or finely vacuolated ambophilic cytoplasm and large vesicular nuclei. There was no intercellular material. Areas of hemorrhage and necrosis were seen. Tumor giant cells and bizarre mitotic figures were found in both of the tumors which infiltrated soft tissue. The bone contained no neoplastic cells (Fig 16). The second recurrence was macroscopically nondescript. The histological characteristics were similar to the highly vascular multicentric part of the parent lesion. Spindle shaped and polygonal cells formed a network about endothelial lined spaces. Variation in cell size and shape, hyperchromatism and mitotic figures were conspicuous (Fig 17).

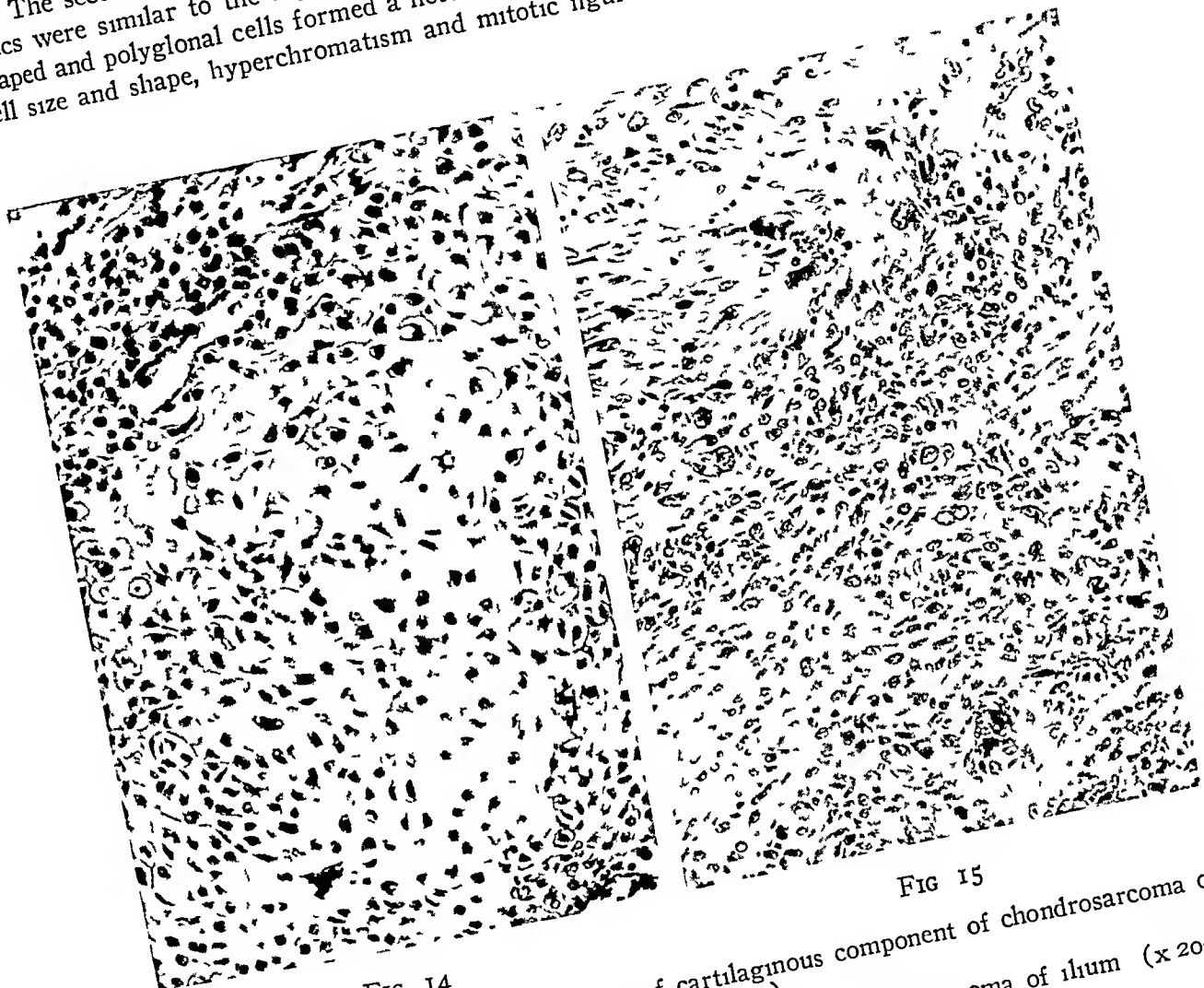


FIG 14

FIG 15

FIG 14 (Case 10) Representative area of cartilaginous component of chondrosarcoma of ilium ( $\times 200$ )

FIG 15—(Case 10) Area of anaplastic sarcoma from chondrosarcoma of ilium ( $\times 200$ )

A gray resilient extraperitoneal mass weighing approximately 2 kg filled the surgically created defect in the ilium at postmortem examination. The tumor extended from the ilio-lumbar ligament to the conjoint tendon encroaching on the pelvis. Neoplastic tissue invaded the last two lumbar vertebrae and the upper portion of the sacrum. Tumor thrombi were found in the iliac arteries and veins which were distorted by the mass. A solitary metastasis 3 cm in diameter was seen in the liver and smaller nodules of tumor were found in the lungs and the right kidney.

All of the structural patterns observed in the surgical specimens of the neoplasm were found on histologic examination of the autopsy material. Only a few of the lung metastases were frankly chondroid. All of the other lesions resembled poorly differentiated fibrosarcoma.

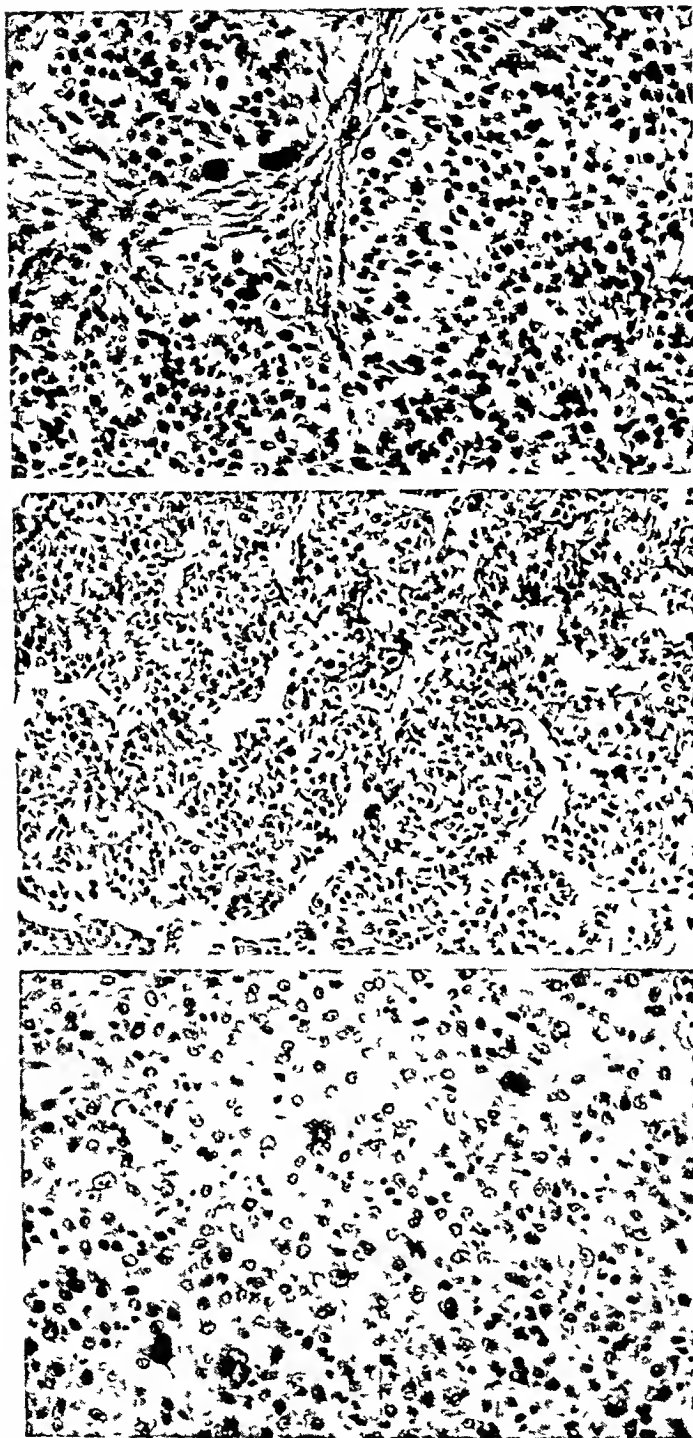


FIG 16

FIG 17

FIG 18

- FIG 16—(Case 10) First metastasis from chondrosarcoma of ilium ( $\times 200$ )  
FIG 17—(Case 10) Intraspinal metastasis from chondrosarcoma of ilium ( $\times 200$ )  
FIG 18—(Case 11) Pulmonary metastasis from chondrosarcoma of pubis ( $\times 200$ )

**Case 11**—No 43193, I D, female, age 51, was admitted to Strong Memorial Hospital Nov 2, 1939, because of increasingly severe pain in her right hip and knee for two years. Masses were palpable in the right lower abdominal quadrant and between the right iliac crest and greater trochanter. Motion of the right hip joint was restricted. The right lower limb was atrophic. An extensive destructive lesion about the acetabulum was demonstrated on roentgen examination. A course of roentgen therapy to the hip did not influence the size of the tumor.

Right interinnomino-abdominal amputation was performed in January, 1940. Convalescence was complicated by wound infection but the patient was in good general condition when she left the hospital two months after operation. In January, 1941, roentgenograms of the chest revealed extensive metastases and death ensued one month later.

*Pathologic Examination*—The surgical specimen consisted of the right lower extremity and the right innominate bone. An ovoid, coarsely nodular, elastic mass 18 x 12 x 10 cm arose from the upper ramus of the pubis above the obturator foramen extending medially and laterally. On cut section the upper part of the pubic ramus was a poorly defined mixture of chalky bone and cartilage. The neoplasm extending from the bone was translucent, gray and rather soft. Some areas were gelatinous. The acetabulum was replaced by tumor and gelatinous material was found in the hip joint. The external aspects of the tumor were covered by tough fibrous tissue continuous with the periosteum but the lesion was not truly encapsulated.

Cellular pleomorphism and poorly formed matrix characterized this neoplasm. Large round or oval cells and smaller fusiform or stellate cells were mixed together. The nuclei were relatively large. Cytoplasm was acidophilic, homogeneous in the smaller cells, vacuolated in the larger ones. Many cells contained two or three nuclei and true tumor giant cells were found. Mitotic figures were encountered infrequently. The watery-appearing matrix contained fine acidophilic fibrils. Occasionally one found small islands of basophilic hyaline ground substance. Lacunae were absent. The tumor was enclosed in a moderately vascular capsule from which septa ran a short distance into the neoplasm but lobulation was not a conspicuous feature in this lesion.

At postmortem examination a large tumor mass weighing approximately 4,000 Gm filled the right lower quadrant of the abdomen. It measured 22 x 20 x 18 cm after a large amount of thick, brown glutinous fluid had escaped from its central cystic portion. The cut surfaces of the mass were firm gray and glistening except for the cystic areas. The mass was firmly adherent to the surrounding structures, infiltrated the gluteal muscles, and surrounded and invaded the resected portion of the sacrum.

The right iliac vein was occluded by tumor thrombus which extended to the lower end of the inferior vena cava. Similar thrombi occluded the larger pulmonary arteries. Grossly visible metastases were seen in the lungs, bronchial lymph nodes, kidneys and spleen.

On microscopic examination the neoplasm found at autopsy was extremely cellular and almost devoid of matrix. The cells were round with large granular nuclei, inconspicuous nucleoli and either finely granular or vacuolated cytoplasm. Hyperchromatism was moderate. Mitotic figures and tumor giant cells were conspicuous. The tumor infiltrated muscle and adipose tissue. The metastases were usually circumscribed but some infiltrated adjacent structures. All of them had the same cytologic characteristics as the pelvic mass (Fig 18).

**Case 12**—No 161737, M M, white, male, age 54, was admitted to the Strong Memorial Hospital, Feb 1, 1940, complaining of pain in the right hip for the past eight years. A tumor had been curetted away from the region of the greater trochanter in 1936 at another hospital. This was followed by roentgen therapy. The lesion recurred slowly, pain became increasingly severe and the hip joint stiff. A huge mass involving the upper left thigh and pelvis was palpable. The left hip was held in 45° fixed flexion and the lower limb was atrophic. There was a draining sinus in the old operative scar. Roent-



genograms revealed a mass surrounding the femur in the trochanteric region with partial destruction of the femur, pubis and ischium

Modified interinnomino-abdominal amputation was performed Feb 7, 1940, from which the patient made a splendid recovery being discharged from the hospital 60 days after entry. Recurrent tumors were excised from the operative site in August and October, 1940. In December he returned to the hospital because of a lump in the left tenth rib which was excised *en bloc*. Widespread metastases eventually appeared and the patient died Oct 3, 1941. Permission for postmortem examination could not be obtained.

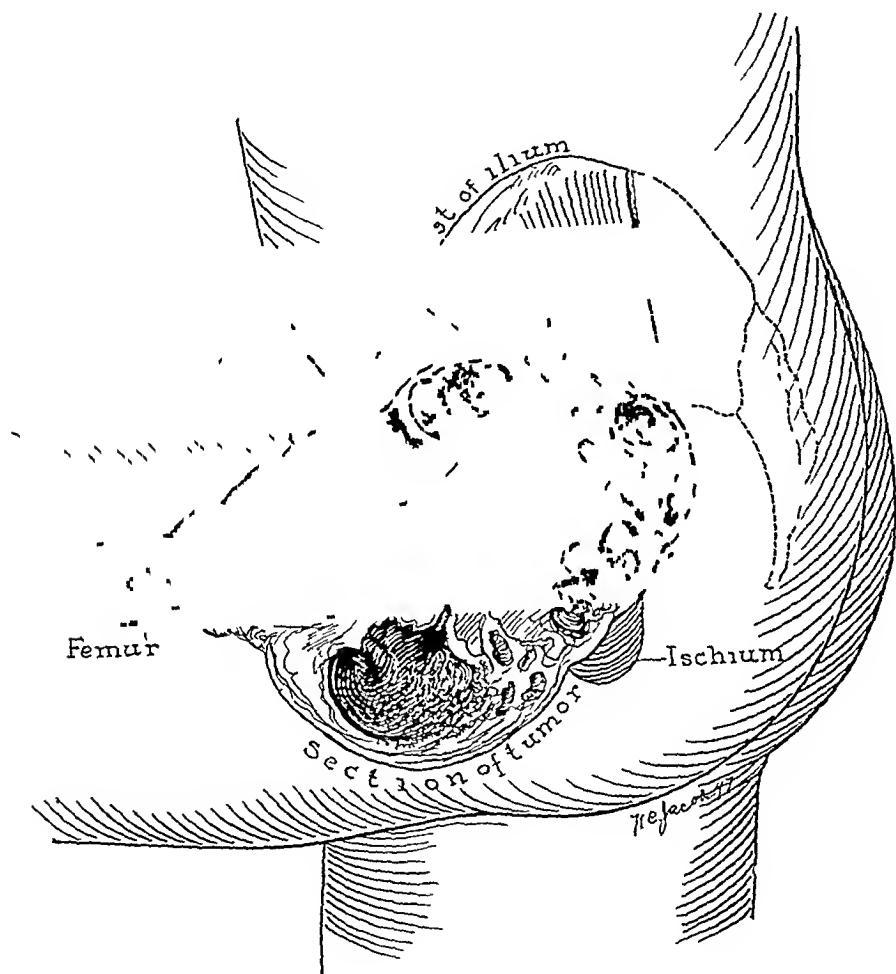


FIG 19—(Case 12) Chondrosarcoma of hip Case 12. The stippled area contained histologically typical osteogenic sarcoma. The rest of the mass was frankly chondroid including the intramedullary extension in the femur.

*Pathologic Examination*—Tissue removed at operation in 1936 contained fragments of atypical hyaline cartilage. Cells were generally ovoid or spindle shaped and the matrix was poorly formed. The nuclei were small and compact. Binucleate forms were seen rarely.

The specimen received after interinnomino-abdominal amputation consisted of the left half of the pelvis and attached lower extremity. The medial half of the pelvis was covered by a gray bosselated tumor mass 20 cm. in diameter which extended over the hip joint to the junction of the upper and middle thirds of the femur. The middle third of the femoral shaft was almost twice the diameter of the lower third. The consistency varied

It was generally firm and elastic but the posterior inferior portion was boggy and that part overlying the ventral surface of the femur in the region of the greater trochanter was stony hard. On section through the pelvis and femur the bulk of the mass was gray, translucent and glistening, obviously cartilaginous. There was a blood-filled excavation 6 cm in diameter in the posterior inferior aspect of the tumor, and the hard area noted above appeared white and fibrous. Part of the ischium and pubis was destroyed and replaced by a mixture of calcareous material and chondroid tissue. Cortical bone in the upper third of the femur was 1 cm thick. The medullary cavity was filled with cartilage. The relationships of the various parts of the lesion are shown in Figure 19.

The great bulk of this tumor was composed of atypical cellular hyaline cartilage in which cellular pleomorphism was conspicuous. Relatively large vesicular nuclei were the rule. Many binucleate forms were present but neither tumor giant cells nor mitotic figures were found. There were large areas of necrosis and irregular deposits of amorphous calcific material. Some nodules were made up of typical myxomatous tissue in which the cells had small round nuclei. The mass was partly surrounded by dense, avascular collagenous tissue from which short septa extended into the tumor, but, in general, lobulation was poorly defined.

Sections taken from the hard white area near the greater trochanter of the femur appeared entirely different. The cells were generally spindle-shaped with hyperchromatic nuclei. Mitotic figures were readily found. Little collagen was seen but many spicules of poorly formed bone were imbedded in the sarcomatous matrix. Much of the tissue was necrotic. Frankly cartilaginous tissue lay next to areas of typical osteogenic sarcoma. Soft tissues about the lesion were compressed but not invaded by tumor.

*Local Recurrence*—This resembled the more cellular areas of cartilage seen in the parent tumor. Matrix was scanty, cells, pleomorphic, and nuclei large, though few mitotic figures and no tumor giant cells were seen.

*Lesion from Rib*—This appeared almost identical with the sections taken from the trochanteric region—frank osteogenic sarcoma.

**Case 13**—H F, No 224081, a 33-year-old married woman, was admitted to the Strong Memorial Hospital on October 2, 1944. She had been a hospital patient in another city since February 3, 1944. Her trouble began six years previously, following the birth of a son. At that time a mass was noted in her pelvis causing her to limp on the left leg. It was decided to try radiation treatment and two courses of deep therapy were given without benefit. She began to get flexion and stiffness of the left hip. In the spring of 1941 she developed malaise, severe nausea, vomiting, and constipation. A colostomy was performed in June of 1941. She was in the hospital for two months. At home she remained in bed another two months and then got about on crutches to a slight extent. After this, she was confined for a period of six months to a sanitarium for general care. She was returned to the general hospital because of urinary retention in February, 1944. A biopsy of the tumor was taken and a diagnosis of chondrosarcoma was made. A second course of radiotherapy was given without noticeable result. She remained on catheter drainage. In April, 1944, an 8-inch incision was made in the left inguinal region and a part of the cartilaginous growth was removed. The surgeon decided that the tumor could not be removed and further attempt was given up. The wound became infected and was left open for drainage. From the time of onset in 1939 there had been progressive loss of sensation and motor control in the left lower limb until she had complete paralysis and sensory loss below the hip joint level.

In her past history there had been little of significance until her present illness. Since 1941 she had had a colostomy which was well regulated until June, 1944. Since that time she had had poor control with large normal-appearing stools per rectum at times. She had had urinary frequency, dysuria, and passage of rather thick purulent material. Her menses had stopped following the x-ray treatments. She had had occasional sharp shooting pains into the left leg.

Her family history was important in that her mother had died of cancer of the breast with metastases in 1937. Her father died in 1916 of a bone disease of the spine, possibly tuberculosis. There was a history of cancer in an aunt and an uncle, the aunt being her mother's sister who died in 1937. The uncle married into the family.

She had the appearance of a chronically ill patient, poorly developed, emaciated, incapacitated. She was cooperative and intelligent. She had pallor of the skin, clubbing of the fingers and toes. The left hip was held in an acutely flexed position at a 45° angle. It was not possible to extend the thigh, but a slight amount of rotation was obtained. The lower leg was flexed and rotated outward. There was loss of muscle power, atrophy, and loss of superficial pain and touch in this limb though deep pressure and vibratory sense were retained. Hip flexion and knee flexion contractures were of considerable extent. There were ulcerations on the left heel. The deep reflexes were not obtainable. A bony hard tumor mass was palpable, extending from the symphysis across the whole left abdomen above the left ilium and around to the sacrum in back. It invaded the gluteal muscles extensively. The abdomen was asymmetrical as the whole left lower portion bulged with a prominent tumor. There was a colostomy opening at about the level of the umbilicus on the right. In the left groin there was a 6-inch (15 cm) gaping wound which was discharging purulent material. Pelvic examination indicated that the rectum and vagina was pushed to the right side of the pelvis. Her temperature was 97.7°F (36.5°C), pulse 98, blood pressure 88 systolic, 48 diastolic. She weighed 88 lbs (40 kilos). The white blood count was 6,100 and the hemoglobin was 10.6 Gm. Her total proteins were 5.44 per cent with 3.56 per cent serum albumin and 1.88 per cent serum globulin. Blood chlorides were 562 mgs per cent, nonprotein nitrogen 27 mgs per cent. The urine contained large numbers of pus cells and grew *Staphylococcus aureus hemolyticus* on culture.

The x-ray appearance was typical of chondrosarcoma (Fig 20).

She was placed on mandelanime in an attempt to clear the urinary infection. She could not take the sulfa drugs as she had a susceptibility which had been determined on her other hospitalizations. She was given a high caloric diet and the infected wound was compressed. Her colostomy was not functioning well and had to be regulated. This therapy took about three weeks, after which it was decided to attempt operation.

An incision was made just to the left of the mid-line from the symphysis to beyond the umbilicus. Many adhesions were freed. The tumor extended across the pelvis into the right iliac fossa. It ran close to the base of the bladder. The uterus was pushed over to the right, the left round ligament being greatly stretched. This was divided. The left tube and ovary were normal, the right ovary was not present. The right ureter was normal. The left ureter ran into the tumor mass and could not be traced. The rectum was full of very hard fecal material, the colostomy being apparently an opening into the side of the transverse colon and not an obstructive type. On the medial side of the rectum there was a mass of gelatinous-like tissue resembling colloid. There was no induration of any sort, but it was decided to take a biopsy in order to rule out colloid carcinoma. The left common iliac artery was exposed and doubly ligated with cotton. This artery was much smaller than the corresponding iliac artery on the right. Closure was made in layers with cotton. The operation was well tolerated. It seemed that a resection might be possible although it was debatable. Many of the staff were positive that the condition was inoperable, a view with which I was in complete accord. The patient and her husband, however, wanted to take any risk as they had nothing more to look forward to. Accordingly on November 1, 1944, eight days later, an inter-innomino-abdominal amputation was carried out. It was necessary to modify the usual operation in several particulars. First, an incision was made in the left groin parallel and medial to the infected incision left by the operation of April, 1944. A flap of skin and subcutaneous tissue was turned over and sutured to the iliac crest completely covering the infected area. A new aseptic procedure was then instituted. A second incision was made through the abdominal wall between the mid-line and the previous inguinal incision. Thin adhesions were separated easily. The symphysis was divided. The tumor extended directly under the urethra from which it was

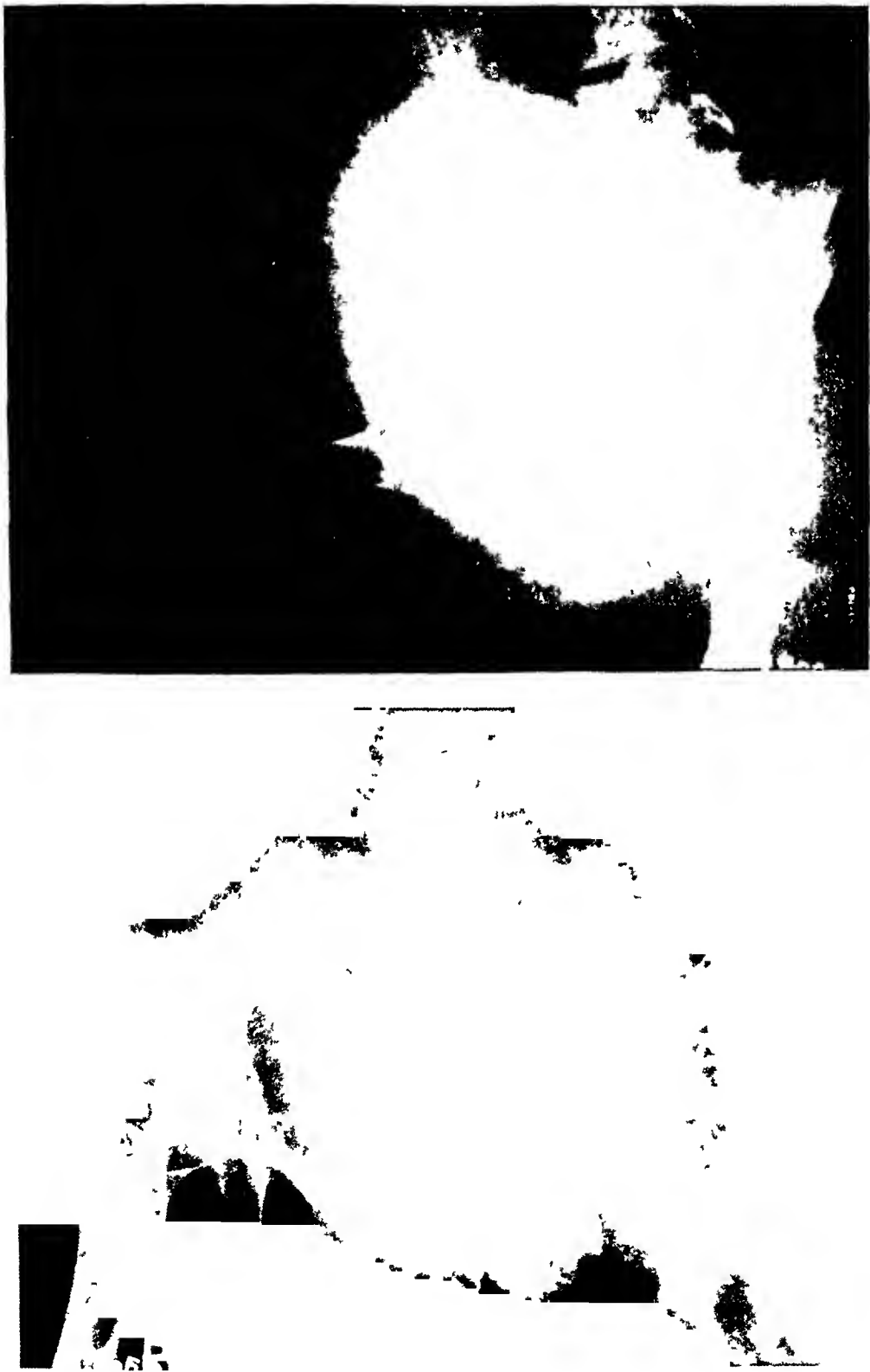


FIG 20 —(Case 13) Roentgenographic appearance of huge chondrosarcoma of hum (Case 13)

dissected free. A pin-point opening was made into the urethra in spite of every precaution. It was repaired at once. The vagina had been pushed over to the right by the tumor. It was entered at one point, but no attempt was made to close it. The left ureter was clamped and divided below the tumor where it entered the bladder. It was identified above the tumor, divided and tied. It contained some whitish cloudy fluid. (Intravenous pyelogram before operation showed no filling of the left kidney pelvis). Then, the patient was turned over on her abdomen, the orthopedic trough making this easily accomplished. It was apparent that the tumor had invaded the gluteal muscles almost everywhere and that these structures could not be used for closure. A flap of skin and subcutaneous tissues was developed from the antero-lateral side of the left thigh and from behind the iliac crest to the mid-line spines posteriorly. This flap was turned over toward the right side. The femoral nerve and the ilio-psoas and levator muscles were divided. The rectum was dissected free from the tumor and pushed to the right side of the pelvis. The sciatic nerve and all the other structures holding the limb were cut across, the incision passing through the left sacro-iliac joint into the great sacro-sciatic notch and across the lower sacral segments. A portion of the left lower sacrum and the coccyx had to be sacrificed with the sacrum. Closure was made by swinging the posterior flap to the incision on the anterior abdomen. The rectum was sutured back into its normal relations. The operation was deliberately performed with a minimum of blood loss under nitrous oxide-ether anesthesia. It took  $4\frac{1}{2}$  hours. There was mild shock after the second hour but with saline and blood intravenously the pressure was on the rise before the operation was completed.

The postoperative course was complicated. She had purulent drainage from the vagina immediately postoperatively. On the 5th postoperative day several firm fecal masses were removed from the rectum, the patient having desire to defecate but not being successful. She had been placed on constant bladder drainage. On the 6th postoperative day she complained of pain similar to that in the left leg before operation. She thought the limb was undergoing twittings or gentle flexion and extension of the thigh. These sensations were not very troublesome usually. However, upon some manipulation such as a dressing or an enema the phantom limb sensations became especially vivid and distressing. She might have a shooting pain to her leg and foot on these occasions. All sutures were removed on the 12th postoperative day. The wound was well healed without infection. There was a slight reddening of the skin flap over the divided edge of the sacrum. She was kept comfortable on codeine and bromides. An abscess formed in the posterior part of the incision and *B. proteus* was cultured from it. It drained profusely. Another pocket was found over the sacrum. These abscesses healed slowly but were healed by the 6th week after operation. She had difficulty with her urinary tract and vaginal infections for about the same length of time. She began to get up on crutches in the 5th postoperative week. This caused her to feel her amputated limb again, in a flexed position as previous to operation. She said that it made her feel tired to hold the limb in this position. She began to gain weight and strength. Her appearance was greatly improved. The colostomy opening continued to annoy her. So after studying the bowel by barium through the colostomy and by rectum, it was decided to close the colostomy. The colostomy was excised and an end-to-end anastomosis made on January 18, 1945. Spinal anesthesia was used. The phantom limb had not been prominent for a couple of weeks. But when she was brought into the operating room after the spinal anesthesia had been given she complained of tingling, "pins and needles" sensations in the limb. She said that it was straight out,—full length. She cried out with sharp pain in the knee joint of this limb. She apologized and said "It is foolish. I know there is no limb there." This sensation lasted about 10 minutes while she had anesthesia to well above the costal margin at the time. She passed gas by rectum on the 4th postoperative day. The bowel functioned normally after this. Convalescence was uneventful. She got about the ward on crutches which she managed nicely. She was discharged on February 2, 1945, much improved with well healed incisions. She had gained 25 pounds since operation.

Postoperative x-rays showed absence of the left pelvis but nothing else of note.

She was readmitted in March, 1946, for local recurrence of the lesion. It was excised and she was discharged in good condition. The tumor was the size of a lime near the coccygeal region.

In August, 1946, she returned with small bowel obstruction. It was released. Another nodule was present back of the rectum. It was friable and broke on attempting to remove it. The area was carbolyzed.

The small bowel attached itself to the carbolyzed area and obstructed again. An enteroenterostomy between the dilated and collapsed loops of terminal ileum gave relief to her obstruction. She was discharged in good condition.

She was admitted to the hospital for the 4th time on Jan. 7, 1947. A recurrence had been noted on examination. She had had some distention with pain, referred to her phantom limb and shooting pains in the stump. Recurrent nodules were removed from the omentum, vagina, wall of the rectum and perineum. One of the recurrent nodules broke on attempting to free it. Following operation she had an infection which gradually collected as a large abscess. It caused severe shooting pain into the phantom limb. Drainage of the abscess was accompanied by complete relief of symptoms and the phantom limb no longer gave her trouble. There were evident recurrences or residual nodules still present but she was discharged for an interval to allow her to recover. It was thought better to defer surgery till her infection had completely burned out.

*Pathologic Examination*—After the soft parts had been dissected away the tumor appeared as a gray bossellated mass of firm tissue surrounding almost all of the left innominate bone. Only 4 cm. of the pubic ramus and a strip of the posterior ilium 6 cm. wide were uninvolved by the mass. The cut surfaces were gray, translucent, coarsely lobulated and marked with small areas of hemorrhage and irregular, stony-hard masses of opaque, yellow-gray, gritty material. Most of the osseous tissue within the mass was completely destroyed. The neoplasm infiltrated contiguous muscle and connective tissues. It extended into the ilio-femoral ligament but did not involve the hip joint.

The tumor was composed of adult type hyaline cartilage with well defined lacunae and hyaline matrix. It was moderately cellular. The cells were ovoid, small at the periphery but larger as one progressed centrally. The nuclei were generally small but in some areas they were relatively large and in these locations one encountered binucleate cells. Cytoplasm was acidophilic, homogeneous in the smaller cells, vacuolated in the larger ones. There were no tumor giant cells nor mitotic figures. Some areas of hemorrhage and deposits of amorphous calcific material were encountered. In some regions calcification was so pronounced that a peculiar osteoid appearance was noted. All of the cells in the heavily calcified areas were small and all of these areas lay toward the center of the lesion. The tumor infiltrated adjacent bone, replaced osseous tissue, and filled the marrow spaces. It also infiltrated soft tissues and had a well defined capsule in only a few areas.

A small subserosal nodule removed from the uterus at operation proved to be an implant of chondroid tumor cells.

The third part of the specimen removed from the wall of the rectum was a moderately cystic lymphangioma. The recurrences were globular masses of tumor cartilage varying from 4 to 7 cm. in diameter. They resembled the parent tumor in all particulars excepting that they were slightly more cellular. All of them contained extensive calcific areas and in the last recurrence there was one nodule which had a bony center in which well defined marrow spaces filled with fat could be seen.

**Case 14**—F. S., No. 1993, a 55-year-old man was admitted to the Rochester General Hospital on Feb. 15, 1929.

He was bowling 15 years ago when he noticed a sharp pain in the calf of the right leg as he stepped forward. The calf was quite painful for the next two weeks but he kept at his work. There was no trouble following this till three or four years later. At that time there was a swelling in the calf. Roentgenograms were taken and a diagnosis of osteo-chondroma was made. There has never been any pain or disability. But during the

last year once in a while he had had to use a pillow under the leg or it would go to sleep. The swelling had grown rapidly in size during the last three months. Trousers made three months ago are a little tight now. He walks well but tires if he walks fast.

He was always healthy. The family and past histories were non-contributory.

He was overweight. The only important finding was a huge tumor of the right calf. It approached the size of a head, was bony hard and fixed.

*Laboratory studies* showed normal blood and urine. Roentgenograms revealed a tumor springing from the posterior edge of the right tibia in its upper third. The cortical bone was thickened and irregular, there were many many scattered calcifications in the tumor which occupied the popliteal space and upper calf.



FIG 21—(Case 14) Chondroma of tibia (Case 14)  
( $\times 60$ )

At operation the tumor was removed locally from the tibia.

Recovery was uneventful. On Sept 13, 1946, he had had no recurrence and was enjoying excellent health. This was over 15 years since operation.

*Pathologic Examination*—The specimen was a well encapsulated, ovoid, firm, gray mass 15 cm in diameter and 12 cm in maximum thickness. It weighed 1,300 Gm. An irregular area of cancellous bone 7 cm in diameter represented the base of the lesion. The greater part of the tumor's cut surfaces were made up of lobulated, gray, glistening cartilage. Many lobules had soft centers from which a viscid material could be expressed. Irregular, chalky white, gritty areas of calcification extended into the cartilage at the base of the lesion where islands of cancellous bone were also seen. The tumor was poorly delimited from the underlying bone. No capsule could be found in this region.

Histologic examination revealed characteristic adult type hyaline cartilage divided into

lobules by poorly cellular, avascular collagenous tissue radiating from the capsule. The tumor cells lay in lacunae, had acidophilic cytoplasm and small compact nuclei (Fig 21)

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DISCUSSION—DR BRADLEY L COLLY, New York We recognize two varieties of malignant cartilage tumors which have different characteristics, such as age-incidence, growth-rate, roentgenographic findings and microscopic appearance. They also have a different prognosis and may require different treatment.

The first of these, occurring in childhood or adolescence, is a highly malignant tumor from the start and, despite amputation, a large percentage of the patients will die of metastasis to the lungs. This form resembles osteogenic sarcoma on the x-ray film and often cannot be differentiated until microscopic sections have been examined. It is termed primary chondroblastic sarcoma.

Doctor Morton's cases, however, fall into the second group which develop on a pre-existing benign cartilage tumor or chondroma, either of central or cortical origin. They are termed secondary chondromyxosarcoma, although the myxomatous element varies greatly and is probably not important.

In the second group the tumor has a more insidious onset. It may be difficult if not impossible to determine just when it ceases to be benign and becomes definitely malignant. We believe that in some instances years may lapse before this transition takes place. This tumor is radio-resistant.

It is our conviction that the presence of a benign chondroma is an indication for removal while it is still a chondroma, this may be regarded as effective cancer prevention. Conservative surgery at this early stage may be sufficient, whereas after a malignant transformation has taken place even an amputation may be ineffectual.

I shall show slides of four patients. In two the tumor was removed while it was still histologically benign chondroma, in the other two, the microscopic diagnosis was that of



chondrosarcoma In all four cases the treatment instituted avoided amputation, in three the follow-up period exceeded nine years

*Case I* Central chondroma, appearance in 1930 Subsequently three separate attempts were made to cure by curettage but each was followed by recurrence (2) Segmental resection of middle of humerus (3) Appearance 18 months later This patient has remained well for ten years

*Case II* Chondromyxosarcoma of scapula, view taken in 1935 Total scapulectomy performed 11 years ago Patient is now well with a useful arm

*Case III* Chondrosarcoma developing in a pre-existing osteochondroma attached to the femur by a rather narrow pedicle (2) appearance after local removal of the tumor, saucerization and chemical cauterization of the base Patient remains well nine years later

*Case IV* Central chondroma of humerus in a 33-year-old naval officer Appearance after five operations and immediately prior to the sixth (2) Resected specimen 15 cm in length (3) Appearance nine days after a tibial transplant to replace the resected area of the humerus This is a recent case operated upon only 16 days ago Histologic diagnosis—benign chondroma

We are indebted to Doctor Morton for presenting this group of cases of a type in which most of us have found in the past that the treatment rendered has been too little and too late Later on when operations of greater magnitude have been attempted the results have been unsuccessful Chondroma must be regarded as a disease possessing serious potentialities

DR KELLOGG SPEED, Chicago My recorded experience covers ten benign chondroma, six of which were the so-called enchondroma of the bones of the hand and foot, and seven malignant chondrosarcoma, including one of the chest well previously reported before this Association Two were of the ilium, for which I performed interilio abdominal amputation, the remainder were in the femur

Two concise statements of Doctor Morton are noteworthy "The microscopic anatomy of chondrosarcoma is extremely variable" and "Many sections are essential" Only by such means may the different histologic aspects, from bony tissue to soft myxomatous areas, be uncovered Codman in 1925 referred to this distinctly in his small invaluable monograph on bone sarcoma His opinion was that no matter what variance of tissue exists—bone, cartilage, or myxomatous, the degree of malignancy was likely to be established by the character of the undifferentiated portion of the proliferating cells, and that the gross appearance and amount of hard tissue might be misleading This is verified by Doctor Morton's report, where metastases showed little if any chondromatous tissue

I wish to show slides, one of a massive slow-growing chondrosarcoma of the femur, ending fatally a year after amputation of the leg, one where amputation was refused and local excision was done with no recurrence up to three years, although chondrosarcoma was diagnosed and, finally, the end result with autopsy findings 13 years later of my patient, included by Doctor Phemister in his report

DR DALLAS B PHEMISTER, Chicago Doctor Morton mentioned my previous description of chondrosarcoma of bone In fact, the term had been in use for more than a generation, but the Committee on the Registry of Bone Sarcoma had refused to accept it I reported a series of cases and pointed out that they could usually be diagnosed from their roentgenologic characteristics, after which chondrosarcoma was listed as an entity in the Registry

My experience with roentgenotherapy has been somewhat different from that of Doctor Morton, in that certain cases have responded well to x-ray A large chondrosarcoma of the ilium, confirmed by biopsy 15 years ago and treated by prolonged and extensive irradiation, has progressed only slightly during the past 13 years and as yet there

are no detectable metastases. A central chondrosarcoma of the upper end of the humerus was extensively curetted 12 years ago and then treated by x-radiation. There has since been no recurrence, an unlikely result had there been no irradiation therapy.

Because of their slow growth and tendency to late metastases, selected cases of chondrosarcoma are suitable for treatment by wide resection and bone transplantation. Several patients have been thus treated and three have remained well for six or more years. In one case, 15 cm. of the shaft of the femur was removed and replaced by two grafts taken from the tibiae seven years ago and there has been complete restoration of function. A similar result was obtained after massive excision and transplantation for a small central chondrosarcoma of the upper diaphysis of the tibia six and a quarter years ago. In the third case, the upper third of the tibia was resected eight and two-thirds years ago and the knee stiffened by bridging the defect with a graft. Resection transplantation is an operative procedure that should be more widely practiced than is the case at present.

DR JOHN J. MORTON, Rochester, N. Y. (closing). I wish to thank all the discussors. I agree with them that if these tumors once recur the patients are candidates for massive resection if it can be done. In the periphery, massive resection with bone graft is excellent.

With regard to x-ray therapy, it is said in the literature that they do respond to x-ray occasionally. In a report from the Mayo Clinic, Desjardine reported two cases because they did respond to x-ray. It is the exception when they do respond, rather than the rule.

## EXPERIENCES WITH A BONE BANK\*

PHILIP D WILSON, M D

NEW YORK, N Y

THE PURPOSE OF THIS CONTRIBUTION is to call attention to the practicality and utility of preserving human bone in a fresh state by means of refrigeration for later use in various operations upon the bones and joints. The method has been used by my colleagues and myself on the Orthopedic Service of the Hospital for Special Surgery in New York since April, 1946 and has demonstrated its value.

### PAST EFFORTS AT BONE PRESERVATION

The idea of preparing and preserving bone for later surgical use is by no means new and probably can be traced back as far as the first experiments with the use of bone transplants by Ollier, who, according to Orr grafted a piece of rabbit's bone into a man in 1859. MacEwen in 1886 had the idea of obtaining bone for transplants from amputated limbs. Poncet in 1887 reported the transplantation of a phalanx from an amputated limb to an ununited fracture of the tibia. The graft healed in place although it did not cure the condition.

In a remarkably prophetic article by Carrell published in 1912 on the Preservation of Human Tissues the author reported his experiments in an attempt to find a "method by which tissues extirpated from the amputated limb of a living animal or a fresh cadaver could be stored during the period which elapses between their extirpation and their transplantation on the patient." His experiments were made with skin, cartilage, glandular tissue and bone and the tissues were preserved in cold storage immersed in Ringers solution or plasma. He concluded that the method was feasible and would prove beneficial.

Gallie in 1918 reported the results of his experiments with the use of boiled bone transplants both homologous and heterogeneous and showed that these were in time absorbed and replaced by living bone. He used them in many surgical operations including spinal fusions and thought they served practically as well as fresh autogenous bone when complete contact of the graft with bleeding bone of the host could be obtained. He prepared plates, screws and pegs from beef bone and used them for fixation in the open reduction of fractures with good results.

Lexer in 1925 reported an end result study of a series of cases in which he had transplanted whole joints and hemi joints obtained from amputated limbs and fresh cadavers. The follow-up study showed that the grafts had survived and although the joints showed remarkable degrees of degenerative changes

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\* Read before the American Surgical Association, March 25, 26 and 27, Hot Springs, Virginia

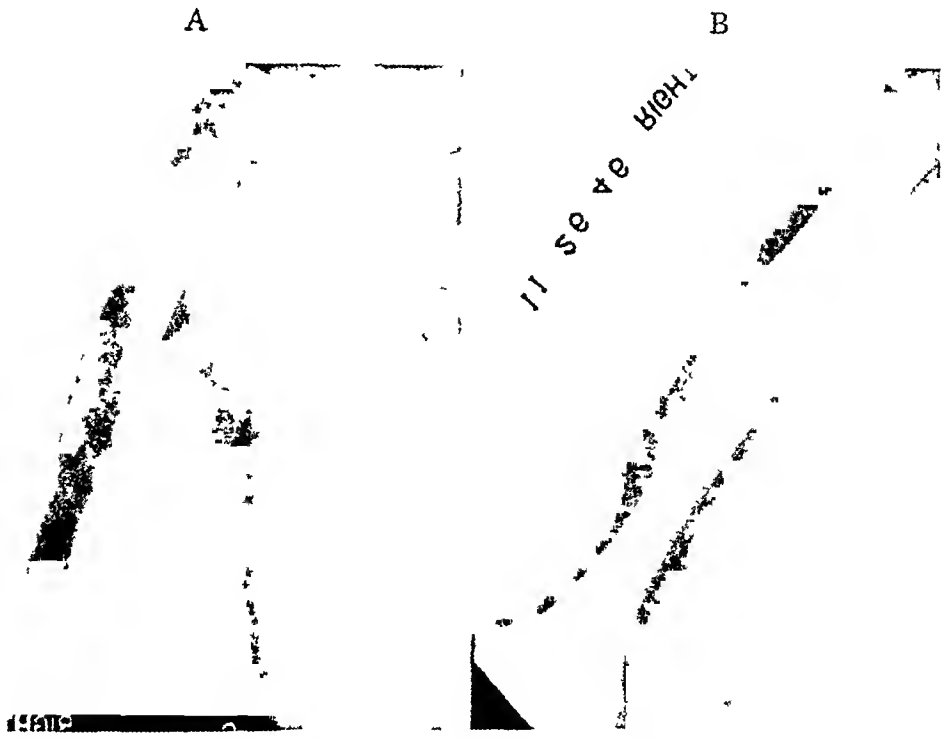


FIG 1—S T Boy, age 11 years Recurrent Hemangioma right humerus (A) 8-18-46 shows appearance prior to operation Operation 9-25-46 Curettage and packing with bone chips after five days refrigeration (B) 11-26-46—the appearance two months postoperative

TABLE I  
OPERATIONS IN WHICH REFRIGERATED BONE WAS USED

	Cases	Number of Operations
Spine fusions		
For scoliosis	7	12
For T B spondylitis	2	2
For congenital paraplegia	1	1
For spina bifida and spondylolisthesis	1	1
For osteochondroma of spine	1	1
For lumbo-sacral instability	1	1
Wrist fusions	2	2
Curettage and packing of bone cavities		
For osteitis fibrosa cystica		
of humerus	1	1
of femur	1	1
For fibrous dysplasia of femur	1	1
For enchondroma		
of femur	1	1
of phalanx	1	1
For hemangioma of upper ulna	1	1
Excision of osteoid osteoma of tibia		
and filling defect with bone chips	2	2
Débridement of chronic osteomyelitic cavities packing with bone chips		
and primary closure		
of femur	1	1
of tibia	1	1
	25	30

and osteo-arthritic reaction, some of the patients had obtained excellent function

Orrell in 1938 reported experiments with the use of chemically treated bone which he called os purum and presented cases showing the results obtained from its use for internal fixation in the fusion of joints and in osteotomies. His studies showed that boiled and dried pieces of bone were transformed more slowly into living bone than autogenous bone and sometimes were not resorbed

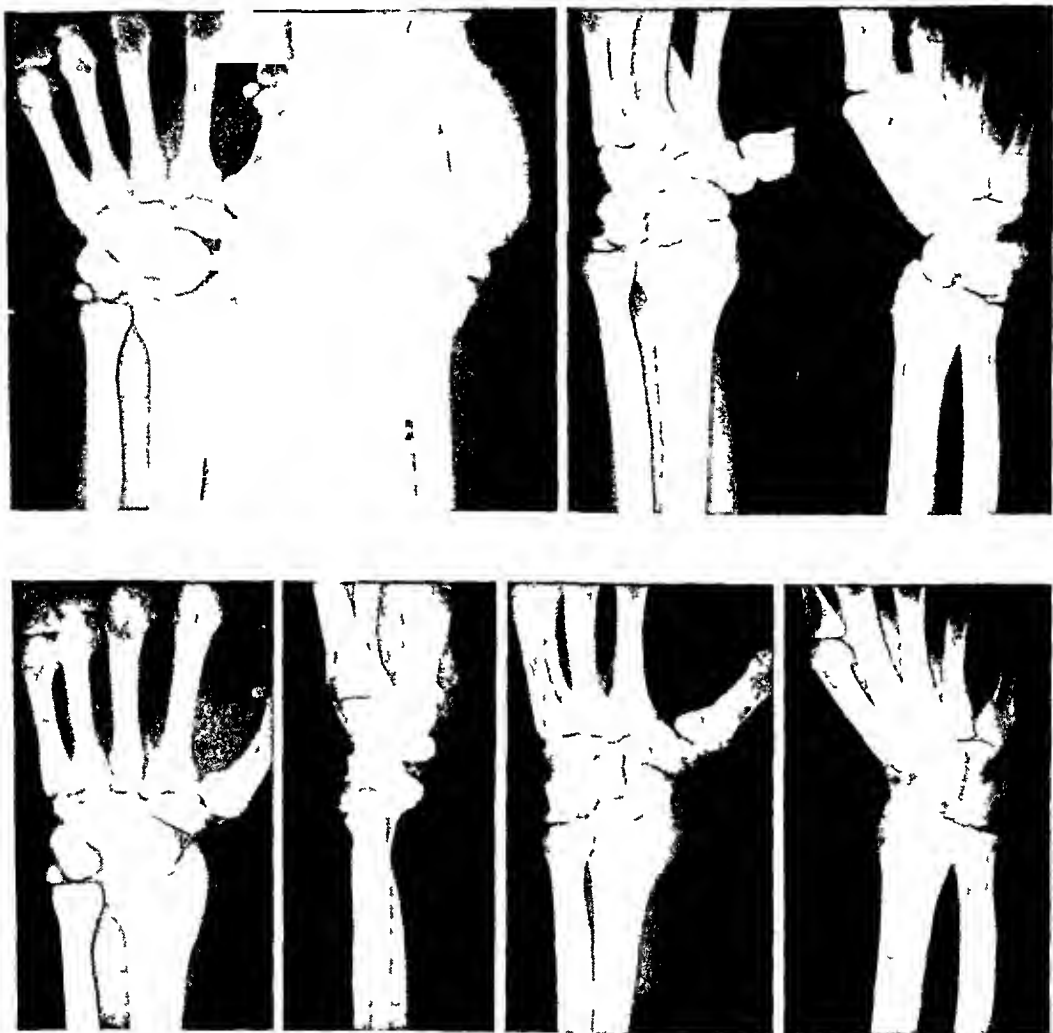


FIG 2—P L Man, age 32 years Diagnosis Old Dislocation of lunate bone  
4-3-46 Preoperative appearance Operation 7-5-46 Excision of lunate bone and fusion  
of proximal carpus to radius with bone chips which had been refrigerated 15 days  
9-25-46 Results 11 weeks postoperative Fusion is solid

at all, probably because the coagulated and dried up connective tissue and collagen were absorbed with difficulty by the host tissues and thus prevented the revascularization of the bone. When these foreign elements were previously removed by chemical treatment the replacement was more rapid.

Inclan in 1942 reported the use of preserved bone grafts in 52 cases. Of

# EXPERIENCES WITH A BONE BANK

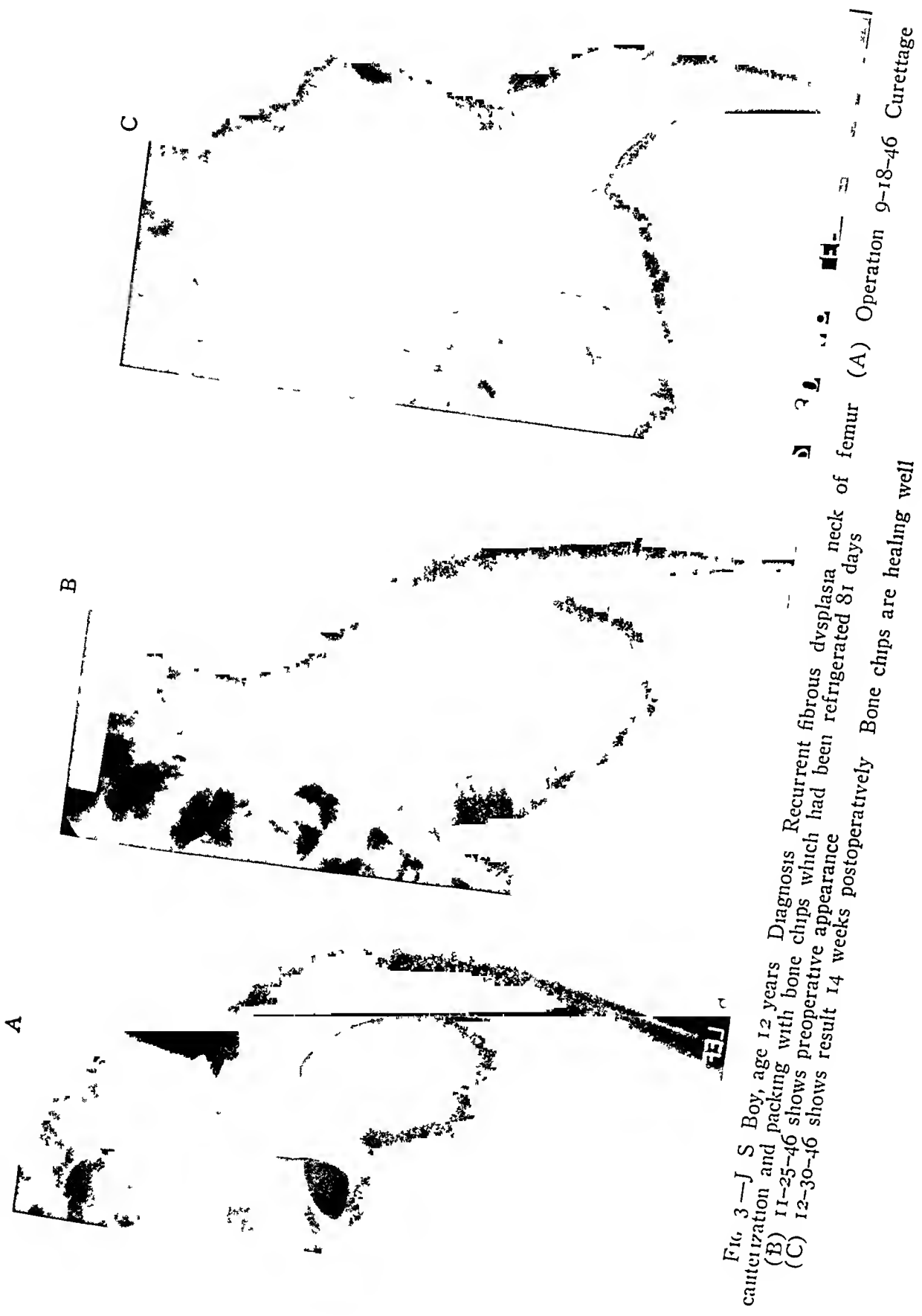


FIG. 3—J S Boy, age 12 years. Diagnosis: Recurrent fibrous dysplasia neck of femur. (A) Operation 9-18-46. Curettage and packing with bone chips. (B) 11-25-46 shows preoperative appearance. (C) 12-30-46 shows result 14 weeks postoperatively. Bone chips are healing well.

these 43 were autogenous grafts previously removed from the patient's own body with the purpose of diminishing shock and risk of infection at the time of the reconstructive surgery, eight were homologous, generally from a member of the patient's family and one was from a nine-month fetus. The bone was preserved in sterile bottles and covered with citrated blood or Ringers solution and kept at a temperature between 2 and 5 degrees centigrade. The period of preservation varied between one and 63 days. Complete success was obtained as far as the healing and physiologic action of the graft was concerned. The results were entirely comparable to those obtained from the use of fresh autogenous grafts.

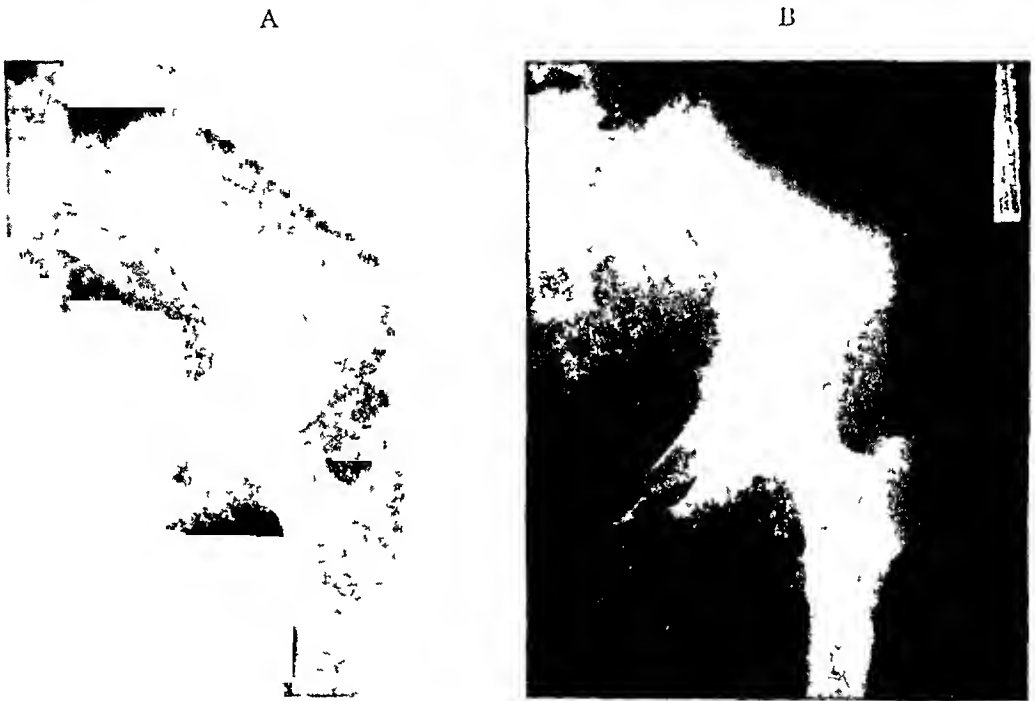


FIG 4—F B Girl, age 17 years. Diagnosis: Bone cyst of Femur. Operation 12-2-46. Curettage and cauterization of cavity, packing with bone chips which had been refrigerated 17 days.

(A) 11-14-46 Preoperative appearance

(B) X-ray 2-14-47—Postoperative X-ray after 11 weeks. The cavity appears completely obliterated by bone.

#### METHOD OF BONE PRESERVATION BY REFRIGERATION

From this very brief and incomplete summary of past attempts to find substitutes for fresh autogenous grafts in surgical operations it is evident that enough success has been obtained to justify further efforts. On any active hospital orthopedic service there is constantly need of bone to be used as transplants in many different kinds of operations including arthrodesis of the various joints, surgical treatment of ununited fractures and filling of bone cavities in various types of benign bone tumors and cysts or in various conditions where excision of bone is required. Until now it has been necessary to obtain bone for such purposes by supplementary operations generally upon the

# EXPERIENCES WITH A BONE BANK

iliac crest or tibia which necessitate prolonging the time of operation, add to the operative risk and certainly increase the patient's discomfort. Not infrequently, the bone defect created by the removal of the graft often in the tibia weakens the bone to such an extent that fracture takes place at some later period.

On the other hand, many orthopedic operations such as osteotomies of the feet or of the bones of the extremities to correct deformities or certain types

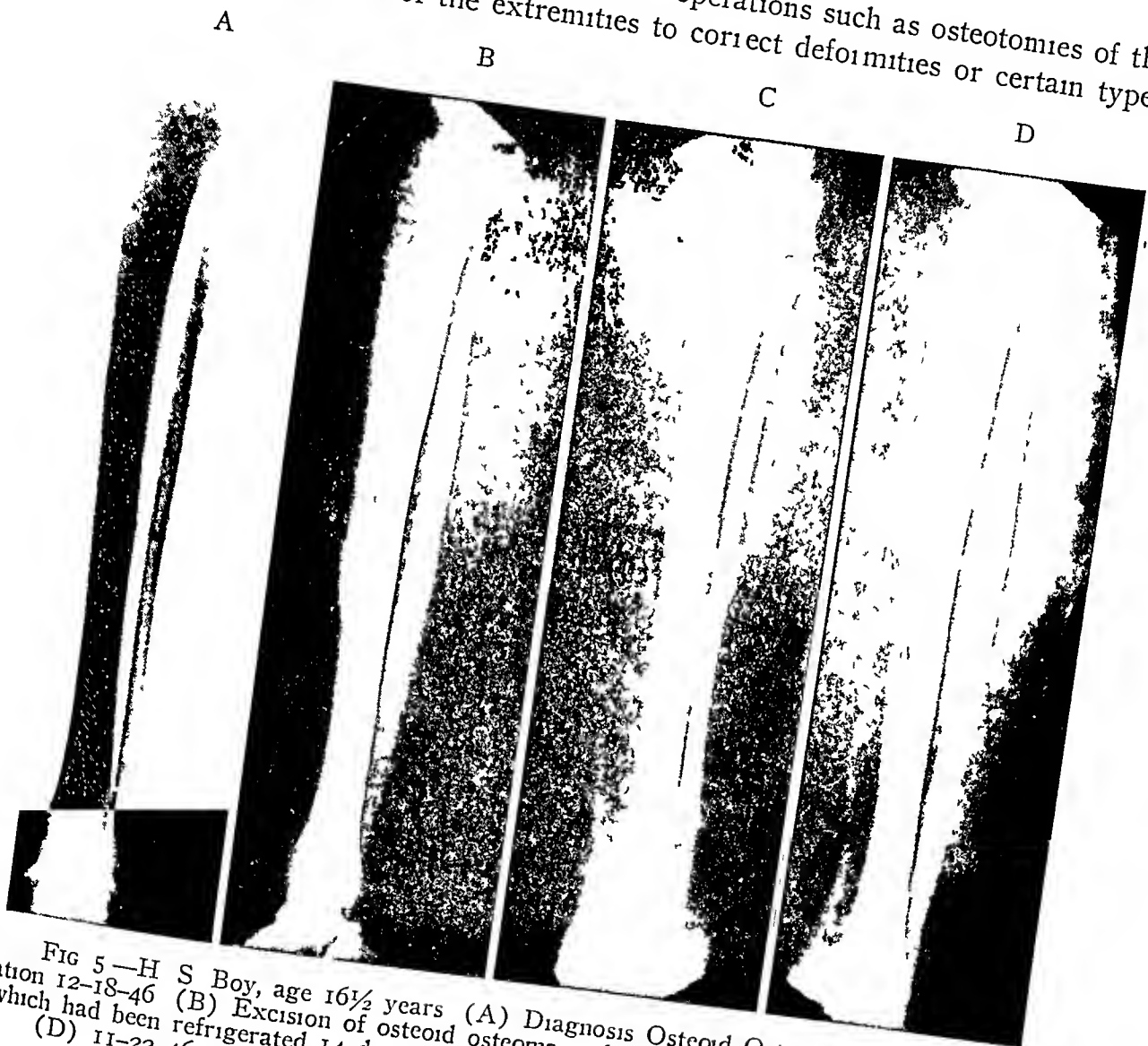


FIG 5—H S Boy, age 16½ years (A) Diagnosis Osteoid Osteoma of tibia Operation 12-18-46 (B) Excision of osteoid osteoma and packing of defect with bone chips which had been refrigerated 14 days (C) 10-29-46 Preoperative x-ray (D) 11-22-46 x-ray appearance of defect 12 weeks postoperative

of arthroplasty necessitate the excision of considerable sections of healthy bone which until now have been discarded as of no value.

It seemed useful to attempt to preserve these fragments of bone for later use as surgical transplants and from earlier attempts and the reports of preservation of other tissues such as eyes, refrigeration seemed to offer the simplest and best method. A deep freeze unit was installed and the bone was transferred to a sterile sealed jar at the operating table and maintained at a temperature of between minus 10 degrees and 20 degrees F. No special effort was made to keep the tissue moist such as by immersing it in Ringers solution.



A

B



FIG 6—R C Man, age 55 years. Diagnosis Chronic Osteomyelitis of lower tibia following compound fracture. Operation 9-9-46 Debridement of sinus and cavity, packing with bone chips that had been refrigerated 89 days. Primary closure with sliding skin flaps. (A) 9-7-46 Preoperative x-ray. (B) 11-22-46 wound healed by primary intention, the x-ray film shows the appearance 12 weeks postoperative.

A

B

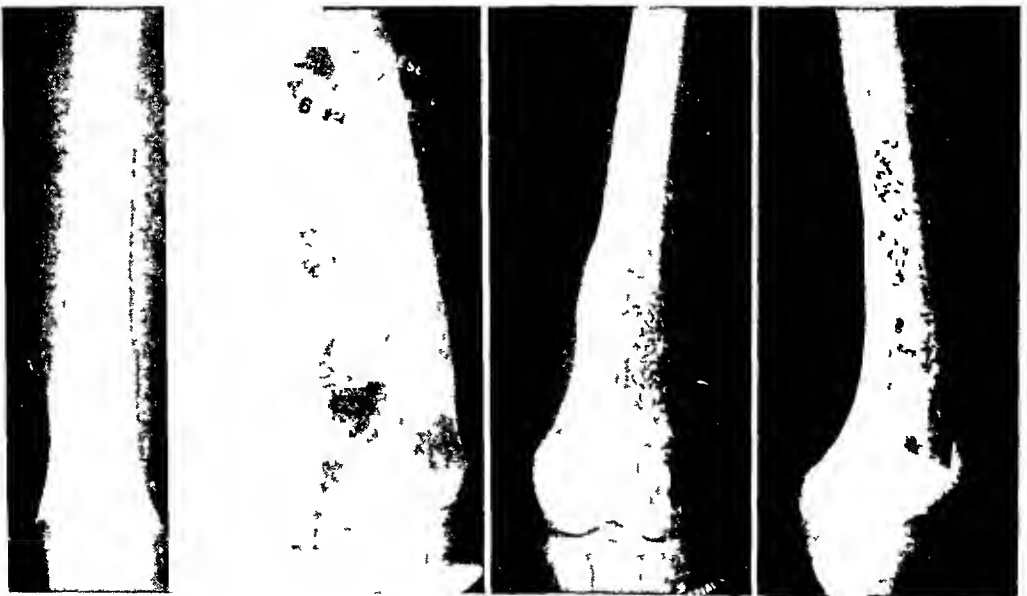


FIG 7—F H Woman, age 34. Chronic osteomyelitis lower end of femur with cavity and sinus six years duration. Operation 12-20-46. Excision of sinus, saucerization and packing of bone cavity with bone chips that had been refrigerated four days. Healing occurred by primary intention. (A) 6-22-46 Preoperative x-ray. (B) 2-8-47 x-ray appearance seven weeks postoperative. Patient has remained entirely well.

## EXPERIENCES WITH A BONE BANK

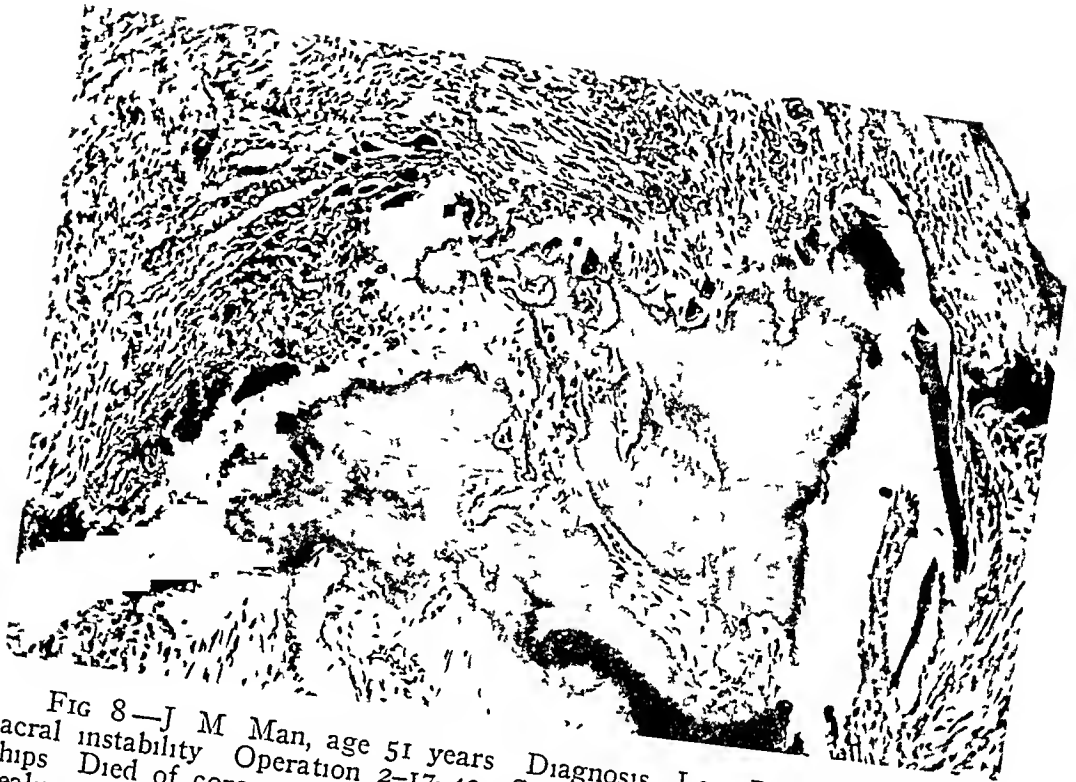


FIG 8—J M Man, age 51 years Diagnosis Low Back pain, lumbosacral instability Operation 2-17-42 Spinal fusion with autogenous bone chips Died of coronary thrombosis 3-12-42 (23 days) A section of the healing autogenous graft is shown and the appearance is that of resorbing dead bone and replacement by living bone from the host

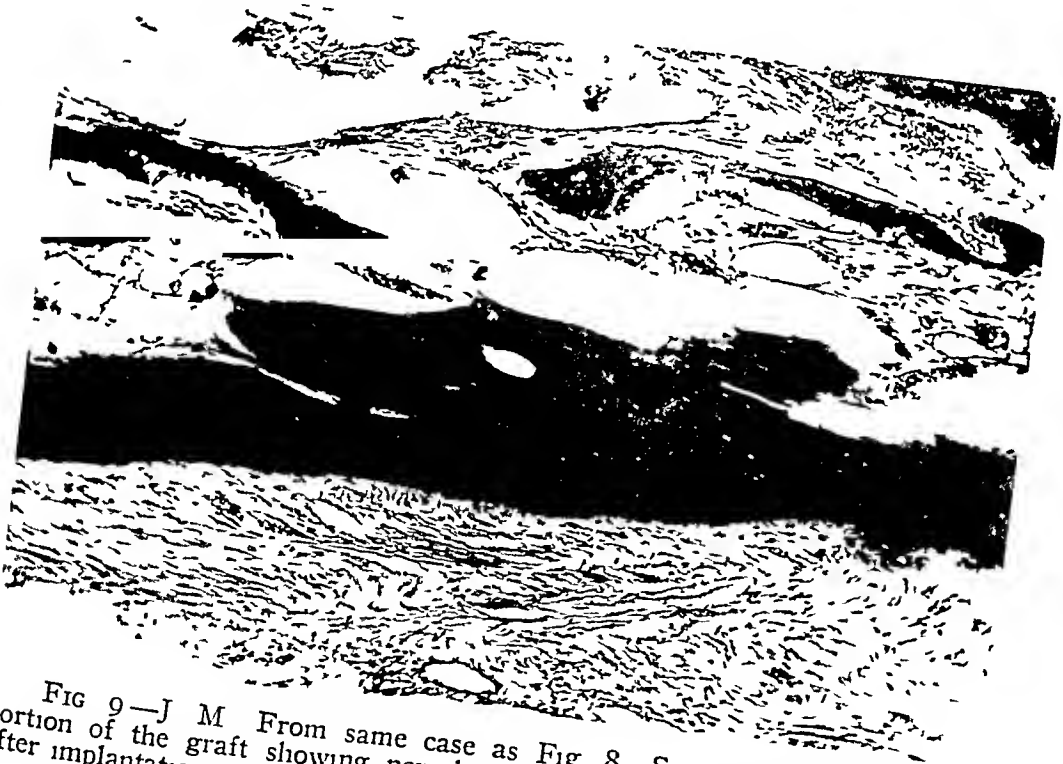


FIG 9—J M From same case as Fig 8 Section through another portion of the graft showing new bone formation on dead bone 23 days after implantation

or citrated blood as it was frozen while still moist and thus preserved its own fluids. Cultures from the bone were taken at the time of bottling and the only other precautions were a Kline test on the blood of the donor to rule out syphilis and a careful check of the patient's history to rule out malaria hepatitis



FIG 10—J P Man, age 28 years, with multiple war wounds of face. Operation 8-23-46. Second stage of nasal reconstruction with implantation of autogenous graft from ilium. Graft became infected and was removed two months later. Illustration shows low power view of graft. Evidence of inflammation which caused graft to be removed is shown at right end. Remainder has been revascularized and is healing.



FIG 11—Same case as Fig 10. High power of section through graft showing new bone forming on dead bone. The appearance is similar in all respects to that seen after grafting refrigerated bone.

or other recent acute infection. Accurate records were kept of the source of the material, the length of refrigeration and the later results after transplantation. We have constantly had in mind the need of adding to our supply of preserved bone and have sought to add to our stock by taking bone from all available sources and particularly from the iliac crest in operations upon the hip when this would not be harmful to the patients.

## EXPERIENCES WITH A BONE BANK

### RESULTS OBTAINED

This preserved bone obtained from 40 different donors has been used for transplantation in 30 surgical operations upon 25 different individuals during the past year. The longest period between the time of removal of the bone and its implantation was 89 days and the shortest one day. The average period of preservation of all the bone used was 42 days. No infections or foreign body reactions occurred and in every case the wound healed by primary intention and remained healed. In no case has there been any sloughing of the preserved bone. Because all of the specimens of preserved



FIG 12—E N Woman, age 16 years, who had idiopathic scoliosis. Following correction a two-stage spinal fusion was done. At the first stage refrigerated bone chips were used and some of these were recovered at the second stage operation. Illustration shows section of refrigerated homologous bone chips three weeks after implantation. Osteoid tissue and new bone are seen forming on the dead bone.

bone were small it was not possible to use them in any form but that of small chips and these chips were used to pack bone cavities or to reinforce various types of fusion operations, especially of the spine. Preferably the bone should be withdrawn from the bank several hours in advance of the time it is to be used in order to allow it to thaw out but in several cases the need for its use had not been foreseen and it was necessary to use it in the frozen state. No difficulty was encountered in these cases however and it is probable that the process of preparing the fragments for use by chopping them up in small bits gave enough time for them to thaw out.

The various conditions and operations in which the bone was used are shown in the adjoining table. Of particular interest were the two cases of chronic osteomyelitis with sinuses, one at the lower end of the femur and the other at the lower end of the tibia. In both there were large cavities in the bone which it was not possible to treat by the ordinary method of extensive saucerization and skin grafting or plastic closure of skin flaps. The amount of drainage was small and of serous character. Careful débridement was done of the sinus and of the walls of the bone cavity exposing healthy bleeding bone. The cavity was washed out with saline, packed solidly with bone chips and then skin flaps were mobilized and closed. The limbs were immobilized in plaster for four weeks. Healing occurred by primary intention and the wounds have



FIG 13—B S Woman, age 25, with Paralytic Scoliosis. Spinal fusion was performed in three stages. At the first operation refrigerated bone chips were implanted which were recovered at the 2nd operation 28 days later. The illustration shows a microphotograph of a section through this bone. Active new bone formation on the old dead bone may be seen. The process seems entirely similar to that seen with the use of an autogenous graft.

remained healed for follow-up periods of three and six months respectively. In one of these cases the bone used had been preserved for 90 days and in the other four days. The uneventful healing in these two cases seemed to prove the absence of any foreign body reaction of the host tissues to the preserved bone.

From a clinical standpoint the results of the use of preserved homologous bone have been entirely satisfactory. In all cases its behavior seemed to be identical to that of fresh autogenous bone. Bone cavities and defects became obliterated and the fusions became solid.

There was one failure in a case of spinal fusion for scoliosis where banked bone was used. Pseudarthrosis was discovered four months after operation.

This patient was reoperated and complete healing of the banked bone was found to have taken place everywhere except at one level where there was a line of pseudarthrosis. This area was excised and refused. Examination of the excised specimen showed the pseudarthrosis lined by cartilaginous surfaces with the adjacent bone showing all the appearance of normal healing.

#### THE HEALING OF REFRIGERATED BONE

Our experience with the use of refrigerated bone and that of Inclan, and of Busch and Garber who have conducted similar experiments show that from a clinical standpoint it behaves in every way similarly to fresh autogenous bone. This raises the question of how such bone acts and whether from a histologic examination of the tissues the healing is also similar.

We have recovered specimens both of fresh autogenous bone and refrigerated bone which were implanted in human spines for the purpose of promoting fusion at a varying number of weeks postoperatively. These were studied and compared with each other by Dr. Milton Helpert, Pathologist at the Hospital for Special Surgery, as well as by myself. We found no evidence that the cells in the bone transplants survived in either case. The lacunar and interosseous spaces of the bone transplants whether fresh or refrigerated were uniformly empty of living cells in the early stages of healing but there soon occurred an invasion of fibroblasts and blood vessels followed by active absorption of the dead trabeculae with large numbers of osteoclasts present. This process appeared to develop from the periphery of the transplant and then to penetrate into the interior. Three to four weeks after transplantation active new bone formation could be seen adjacent to the old trabeculae with both osteoid and osseous tissue present and many osteoblasts arranged about the latter. In other words the healing process seemed comparable in both the fresh autogenous grafts and the refrigerated bone grafts and whether the material was homologous or autogenous seemed to make no difference.

We examined sections of refrigerated bone after varying periods of preservation. The cellular tissue appeared intact and had the same staining reaction as that of fresh bone. This did not mean however that these cells were still alive any more than a normal cellular appearance or staining reaction of a piece of refrigerated steak would mean that that tissue was alive. It only indicates that the tissue is preserved in a fresh state by refrigeration. In short our views conform to those of the many other students of the function of bone transplants who have concluded that the grafts die and are then transformed into living bone by the processes of resorption and osteogenesis of the hosts tissue. In fresh grafts some cellular elements may survive but these are few and not of much importance.

We believe that the advantages of refrigerated bone lie in the fact that it is preserved in a fresh state and therefore that the processes of invasion, resorption and transformation take place more easily than with boiled or dried bone where the organic elements are dried or coagulated as pointed out by Orrell. Whether or not sterile refrigerated heterogeneous bone would serve

as well as homologous bone remains to be determined Obviously there is a large field for further experimentation to answer this and other questions

#### ORGANIZATION OF A BONE BANK

It is only one year since the establishment of a Bone Bank at the Hospital for Special Surgery but in that short time it has proved of great advantage The method of preservation by refrigeration is simple and beyond the initial cost of a deep freeze unit of sufficient capacity, requires no large expenditure We have experienced no great difficulty in maintaining a stock of bone sufficient for routine needs By using this bone we have been able to save a number of patients from supplementary operations and disabilities But thus far the bank has been organized on a small scale and has served only for the purposes of experimentation and demonstration We have not yet attacked the real problem of obtaining and preserving large specimens of homologous bone in order that the needs of surgeons for massive grafts of every description such as may be required for the treatment of ununited fractures or defects created by the excision of tumors and other lesions may be met

For this organization on a large scale is necessary While amputated limbs may supply some of the need, this source is uncertain and generally unsatisfactory because of the pathologic condition which necessitates the amputation Because of lack of knowledge of the survival period of tumor cells under refrigeration, we have not yet felt safe in using bone from limbs which had been amputated for malignant tumors The real solution lies in obtaining bone from fresh cadavers where death has occurred from other cause than infection The material should be removed by an operating team under sterile precautions within six hours, probably longer if the body is placed in cold storage, immediately after death

But the obtaining of fresh bone from this source is hedged about by legal difficulties since the dead body is the property of the next of kin and the time required to obtain that person's consent may exceed the time limit within which the desired material should be removed Even testamentary disposition of his body by a person before death, I am informed, is of no legal value without the signed approval of the next of kin

The experience of the Manhattan Eye Bank shows, however, that many of these difficulties can be solved By means of public education and the cooperation of many persons including physicians scattered throughout the country and the airlines, they have brought forth many donors and insured a supply of eyes which have met most of the current surgical needs for corneal transplants both in New York and other neighboring cities and have also supplied material for important research

While the organization of a bone bank on a small scale such as the one I have described is possible and desirable in every hospital with an active bone and joint service, it seems to me that we should aim for the larger goal of supplying the needs of all surgeons requiring bone for every type of transplantation and that we should take a leaf from the book of experience of the



## EXPERIENCES WITH A BONE BANK

Manhattan Eye Bank and plan to organize a Bone Bank on a community level. In this way the cooperation of all persons both medical and lay would be obtained as the service would be available to all. It probably could subsist on a system of voluntary contributions from the recipients in the same manner as the Manhattan Eye Bank.

### CONCLUSIONS

1 The preservation of fresh homologous bone material by refrigeration for later use in operations upon the bones and joints is safe and practical.

2 As nearly as can be determined both by clinical and histologic study the behavior of such bone after transplantation is similar to that of fresh autogenous bone.

3 In both cases the bone is resorbed and transformed into living bone entirely as the result of the action of the host tissues.

4 Our experience at the Hospital for Special Surgery with a bone bank organized on a small scale after one year of operation demonstrates the need for organization on a much larger scale, of a community Bone Bank to supply the needs of surgeons for bone transplants of every size and description.

DISCUSSION—DR W. E. GALLIE, Toronto. I have listened to Dr. Wilson's suggestion with the greatest interest, for I feel that in it there may be a contribution of much practical value.

He referred to some experimental studies which I reported nearly thirty years ago, in which it was shown that bone, either autogenous or heterogenous, when boiled and placed in intimate contact with living bone, will adhere to it, acquire a circulation through the old Haversian canals, and ultimately undergo absorption and replacement as a result of invasion by living osteoblasts from the surrounding living bone. A superficial examination of such specimens might make one think there is little or no difference in the fate of boiled as compared with that of unboiled autogenous grafts. A more careful study will show, however, that in the case of the boiled grafts there are no living elements whatever, whereas in the case of autogenous grafts, although all cells in lacunae die, nevertheless those osteoblasts which lie on exposed surfaces rapidly multiply and take an active part in the creeping replacement of the graft. This is best seen in experiments where grafts are transplanted from the radius or ribs into the muscles of the back. If the grafts are not boiled they quickly become vascularized and undergo absorption and replacement with new bone, due to invasion by living osteoblasts from their own surfaces. If, on the contrary, the grafts are boiled before being imbedded in muscle, no such absorption and replacement occurs.

The outstanding difference between the autogenous unboiled graft and the boiled graft, when placed in contact with living bone, is that in the latter the process of union, revascularization and absorption and replacement are much retarded. It is because of this that when bone grafts are indicated, autogenous unboiled bone is much to be preferred.

Now, whether bone transplanted from one patient to another would retain any living elements I do not know. Our experiments on animals showed that in transplantation from one animal to the muscles of another animal of the same species, osteoblasts on the surface of the bone sometimes did live, but not always. If the animals were of a different species, no living elements survived. So it may be possible that bone obtained from one patient and transplanted into another may have the properties of autogenous grafts.



Now, whether refrigeration will destroy all the surface osteoblasts is not certain. Dr. Wilson thinks that no living cells survive the refrigeration. It would be interesting, however, to settle this question by the simple experiment of securing autogenous grafts, then refrigerating them for varying periods of time, and then transplanting them into the muscles of the same animal. This should settle whether refrigeration kills the surface cells or not.

No matter what the answer is, however, it is quite possible that bone prepared and preserved as Dr. Wilson has described, may prove to be very useful. This would be particularly the case in filling large cavities. Where the purpose of the graft operation, however, is the overcoming of nonunion or the bridging of gaps, I think the use of refrigerated bone should be supplemented by the ordinary method of using fresh autogenous bone. This limitation would, of course, be removed, if it is shown that surface cells survive refrigeration.

Dr. Wilson's suggestion is highly interesting, and is sure to stimulate renewed interest in the important subject of the transplantation of bone.

DR PHILIP D WILSON, New York (closing). I wish to thank the various members for their questions which I shall endeavor to answer. We did not pay any attention to blood groups in the use of material from our bone bank. Dr. Inellan laid considerable emphasis on this in his work and thought that the donors of grafts should be in the same blood group as the donee. The only thing I can say is that we experienced no reactions thus far. It is possible that if we used more massive grafts which would contain a good deal of protein material, there might be some reaction.

To the question as to whether we have experienced infectious hepatitis in any of our cases, the answer is no. In this connection, I might point out that the donor material is preserved separately and that there is no pooling of the donor material as in the case of pooled plasma. In other words, there should be no more chance of transmitting infection of this kind by the use of bank bone than by individual transfusion.

I am very grateful to Doctor Berry for his suggestion that resected portions of ribs which are frequently obtained by operations on the chest might make a convenient source of material for the bone bank.

I wish to thank Doctor Gallie for his discussion, as he has done much work on the use of homologous and heterogenous bone grafts. In looking over the work of other students on bone regeneration, I find considerable difference of opinion. Some believe that certain of the host elements in a graft survive and proliferate while others do not. There is obviously much room for further experimentation before we have all the answers, but I think that Inellan's work has proved that refrigerated bone in the form of massive grafts will work, and our own experience with the use of smaller fragments of bone certainly has been helpful in many cases and encourages us to go on and expand the method of preserving bone in a bank for general use.

## PENETRATING WOUNDS OF MAJOR JOINTS\*

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EVER SINCE THE ADVENT and acceptance of the principles of asepsis, as established by Lord Lister, and the fundamental concepts of the healing of wounds put forth by Halsted, the interest of surgeons in trauma and repair has varied directly with the occurrence of war. In periods of peace a modicum of experimental and clinical work on this most basic problem in surgery continues, but with comparatively little attention by most surgeons. Rather their interest seems to be centered on the great panacea—elusive as the alchemists' dream of the conversion of base metals into gold—that will heal wounds in spite of neglect of the underlying principles of wound repair. Once Pandora's box is opened, however, and the woes of war suddenly unleashed, the problems posed by wounds become of paramount importance. Symposia are held and old truths hailed as great discoveries, and the currently fashionable wound antiseptics are exploited to their full. Yet what has been their fate, phenol, corrosive sublimate, iodine, Dakin's solution, B. I. P., the newer mercurials, the sulfonamides, and the antibiotics?

"The almost inherent urge to place some agent, with hopeful healing and anti-infective properties, in a wound seems to be deep-seated in the human breast and is as difficult to control as the better recognized human impulses. Time and experience have repeatedly demonstrated the inefficacy of such agents. Perhaps some day such an agent will be found but the search seems futile when it is realized that the key to wound infection in traumatic wounds is dead tissue, a fact which Botallo recognized almost four centuries ago, and which Lister fully appreciated."<sup>1</sup>

Many of the anti-infective agents are of immeasurable aid in controlling infection and extending the scope of surgery, but they are always ancillary to thorough and careful surgery. It took the British three years to recognize this in World War I and in their *Official History of the War* the development of the methods used in treating wounds of joints is divided into four phases.

<sup>1</sup> In the early stages of the war attention was focused on incision and drainage with large tubes. With the exception of a few simple perforating wounds, suppuration was the rule with a resulting high mortality, and an amputation rate of 60 per cent for knee-joint cases with only soft part injury, and 80 per cent for those complicated by fracture.

<sup>2</sup> Early in 1915 the treatment outlined by Colonel H. M. W. Gray was adopted. This consisted of (1) adequate immobilization of the joint, (2) excision of infected soft parts, (3) lavage of the joint cavity after removal of

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the projectile, and (4) closure of the capsule of the joint. If suppuration was present arthrotomy was performed and drainage established only down to the joint cavity.

3 In the summer of 1916 the Carrel-Dakin method of treating wounds was adopted by the British Army and for the first time the importance of early excision of infected tissues as an essential feature in wound treatment was realized.

4 In the Spring of 1917 early and free excision of the injured area was the standard method of treatment with primary or delayed closure of the wound. This resulted in 70 per cent healing by first intention in all wounds. In joint cases only 12 per cent suppurated, while the amputation rate fell from 25 per cent to 7 per cent and the death rate from 15 per cent to 8 per cent.<sup>2</sup>

In World War II, notwithstanding the knowledge already available, much had to be rediscovered. The absolute necessity of wide exploratory arthrotomy and careful débridement of all wounds involving joints, was not fully appreciated at first. This was probably due to our unfamiliarity with the British experience in World War I, and with our own findings at that time, as stated in an admirable article by Pool in the *Medical Department of the United States Army in the World War*,<sup>3</sup> which was not published until 1927. We knew little, and that largely condemnatory, about primary resection of joints and the timing of secondary resection for suppuration. Yet these procedures had all been considered in detail by Pool.<sup>3</sup>

Early in 1943 the Ninth Evacuation Hospital came to the conclusion that all cases of penetrating wounds of joints should be widely opened, carefully debrided and the foreign bodies, debris and blood should be removed. Also the joint should be irrigated with saline, and the capsule closed. The closure of the capsule was thought to be so important, that if a gap existed a sliding flap of skin or fascia was employed.

Complete immobilization of the joint was of paramount importance and in the case of a knee joint this was accomplished by means of a hip spica. The delayed primary suture of the soft parts was performed four to seven days later. When penicillin became available this was placed in the joint in the dosage of 10,000 units at the conclusion of operation. It was repeated at 24-48 hour intervals thereafter for two or three doses, and the patient was also placed on systemic penicillin.<sup>4</sup>

At about the same time, this hospital unit, which was functioning near Naples, admitted a group of French soldiers with well-established suppurative arthritis of the knee. A lower thigh amputation was necessary as a life saving measure in one instance and it appeared that this would be required in five other cases. At the suggestion of Colonel Etienne Curtillet, the French surgical consultant, five resections of the joint were performed. This seemingly radical procedure had been advocated 75 years ago by Ollier.<sup>5</sup> The sepsis subsided and healing was prompt in all five cases, only one case failed to develop solid fusion.<sup>6</sup> These conceptions of treatment were immediately extended to all the hospitals in the Naples area by the teaching and work of Lieutenant Colonel Oscar Hampton and Major Champ Lyons with the cooperation of the various

orthopedists,<sup>7</sup> and further, the principle of re-débridement in the presence of sepsis was established by them<sup>14</sup>

As a result of this early experience a detailed description of the treatment of penetrating wounds of joints was included in Circular Letter Number 2 of the Surgeon of the Seventh Army just prior to the Southern France Campaign<sup>8</sup> The response was more than gratifying and reports came from both the forward and base installations that these wounds healed cleanly when so treated and the only ones that became septic were those that had been neglected or in which débridement was inadequate, usually by new and inexperienced surgeons Two of the Evacuation hospitals reported their results of arthrotomy and débridement of penetrating wounds of the knee joint in detail Of the 227 cases treated by them, two were suppurating at the time of the initial débridement—one 10 and the other 14 days old None of the others showed any signs of infection when evacuated to the rear three to seven days after débridement There were no amputations in this group<sup>9</sup>

In the ancient and modern history of military surgery, there has accumulated enough experience in the treatment of knee-joint wounds to give us confidence that our problem, to a limited extent, is solved We now realize that if these wounds are given the proper primary treatment, suppuration will rarely develop

The same happy outlook cannot be said to apply to wounds of the hip joint There has always been considerable difficulty in obtaining accurate statistics on the incidence of wounds of this joint The proximity of the hip to the femoral and iliac artery, as well as to the bladder and rectum, makes it likely that in many instances death supervenes promptly This may account for the fact that compound penetrating wounds of the hip-joint were not as common a finding in the forward Army hospitals, as were the knee-joint wounds On the other hand it is safe to assume that a projectile may produce tears of the capsule of the hip-joint, or lesser fractures of the head and neck of the femur, and still remain undetected as hip-joint injuries.

Regardless of the number of compounded wounds of this joint that are seen in either war or in civilian practice, they are likely to be tragic when they occur

We have been unable to find any worthwhile contributions to the literature on this subject since the published work of Lagenbeck<sup>10</sup> and Otis<sup>11</sup> 75 years ago Lagenbeck had collected 132 cases during the Franco-Prussian war, and had seen or treated most of them He speaks of three forms of treatment—the conservative, resection of the head of femur and disarticulation of the hip His conservative treatment was definitely the most effective There were 88 cases in this group, 63 proved fatal A mortality rate of 71 per cent! Resection of the head of femur was attended by a mortality of 83.9 per cent, while disarticulation at the hip joint as a mode of treatment caused death in each instance

A review of his cases in the conservative group leaves the impression that his treatment consisted in the main of probing the wound, immobilization and

hot poultices. There is no mention of débridement as we know it today, and no wide exposure of the joint.

Many of his recorded cases were not suspected of having hip-joint involvement during the early period after injury. They were transported to distant hospitals, and it was only after the manifestations of suppuration became obvious that the diagnosis was made. In spite of his figures he favored primary resection of the head of the femur before suppuration had a chance to develop. His belief was that under these circumstances the mortality rate would be lower than in the conservative group.

Otis was very sanguine on the subject of hip-joint wounds in general. He hardly saw a case of recovery of a gun-shot fracture of the hip-joint by expectant treatment, which did not leave a doubt in his mind in regard to the correctness of diagnosis. (This was of course before the days of x-ray.) He arrived in consequence at the conclusion that the expectant treatment must be rejected in all cases, as soon as the nature of injury to the hip-joint became evident. He also favored resection of the head of the femur as the treatment of choice.

In the British medical history of World War I<sup>2</sup> there was an estimated mortality of 60 per cent for all wounds of the hip-joints. Débridement, closure of the joint capsule, and removal of the femoral head if badly comminuted, were advised<sup>12</sup> as the primary treatment. Where sepsis was already established the head was excised routinely and wide drainage obtained. If excision failed, the leg was amputated through the hip-joint. The end results in all cases who survived without amputation were poor, with a grave loss of function and severe crippling.

The medical history of the U. S. Army in World War I<sup>3</sup> devoted little or no attention to its experience with hip-joint wounds, other than to point out their serious nature. The very lack of comment implied an inability to answer the problem. In contrast, the treatment of knee-joint wounds was clearly detailed, and today serves as a model. Any improvement in results, in the treatment of knee-joint wounds in World War II must be credited to the general advances in the surgical adjuvants, and not to changes in the underlying surgical principles.

It became evident to one of us (F. B. B.), as Surgical Consultant of the Seventh Army in France, that the surgical principles which were being so successfully applied to knee-joint injuries, were being ignored in wounds of the hip. Unlike the knee, a thorough exploration and débridement of a hip-joint is a formidable procedure in a severely wounded patient. And yet, if the principle of débridement is valid for the knee, all the more reason it should be applied to the hip with its deep location, its many adjacent muscle bellies and planes, all favoring the development of infection.

It had been observed that on the rare occasion when a hip-joint was explored it was through enlargements of the wound of exit or entrance, which naturally gave a limited exposure to the entire joint. Unlike the knee, the hip is so deeply placed that a simple anterior, lateral or posterior incision will not

lay bare all its secrets. The operator could not end his procedure with the sense of satisfaction that all devitalized muscle had been excised, and that the area had been thoroughly cleansed and freed of all foreign debris.

If he glimpsed the capsule of the joint it was at the bottom of a deep hole, and only a limited portion was in his field of vision. The intricate pattern of overlying muscles does not lend itself to bold incisions, which require only an inch or two more in length to get a good look at the pathology. Boldness of this sort would result in damage that in turn might produce ischemia, or paralysis and atrophy to muscle groups.

In March, 1944, several Evacuation Hospital surgeons in the Seventh Army were requested to perform arthrotomies on all suspected penetrating hip-joint wounds. The operation was to be performed initially, or within a 72-hour period, whenever the condition of the patient permitted. The arthrotomy was to be a formal procedure which would give wide exposure to the joint. Considerable thought was devoted to the type of incision which would give the best exposure, and yet avoid being too destructive. It was agreed that the Smith-Peterson incision was best suited for this purpose, and that if the posterior and inferior portions of the joint needed attention that the Langenbeck or Kocher incisions could be employed separately or in addition. The wounds of entrance or exit were to be incorporated in the incision if convenient, and otherwise they were to be debrided individually.

In April, 1945, one of us (J. E. T.) had his first opportunity to put this plan into effect. The first case was most convincing in two respects. First, that the Smith-Peterson incision gave excellent exposure of the anterior and superior aspects of the joint, and that palpation of the remainder of the capsule would determine the need of an additional posterior incision. Second, the extensive deep destruction to the gluteal muscles could never have been properly débrided by means of any other incision. An infection developing in this situation would have extended directly into the opened joint.

Within a four-week period leading up to the end of the hostilities in Europe, we operated on nine hip-joint wounds. Seven of the nine cases had penetration of the joint capsule, and the remaining two had contusions of the capsule without frank penetration. Contusion of the capsule was considered by Langenbeck<sup>10</sup> to have serious potentialities.

Six of the patients were American soldiers, and three were German prisoners of war. (We have a limited follow-up on all the Americans which has been added to the case reports. No information on the Germans has been obtainable.)

In six cases the typical Smith-Peterson approach was used, and in one a modification of it sufficed. In this latter case it was only necessary to lengthen the wound of entrance on the antero-lateral aspect of thigh, up to the anterior superior iliac spine, and then for an inch along the crest, only detaching the tensor fascia muscle. In two cases the Langenbeck incision was employed.

The nature of the Smith-Peterson incision demanded that its horizontal portion be closed in all layers. The tension was so great on the re-sutured

gluteus medius muscle, that the overlying skin was closed to give it additional support. The remainder of the wound was left wide open, with the expectation that a secondary closure would be performed within a week at some hospital in the rear.

Drainage was used in only one case, the drain was brought out through a posterior stab wound, splitting the gluteus maximus muscle in the line of its fibers.

Dry, fine mesh gauze was used as a dressing over the raw wounds, and in each instance a hip spica was applied. Every case, when possible, was evacuated to the rear within a 48-hour period. The purpose of early evacuation was to have the patient in a permanent installation, in the event suppuration developed.



FIG 1-A—An x-ray of pelvis in Case 1, taken 21 months after injury. The slight upward shift of left half of pelvis can be seen.

All of the patients in the following case reports were admitted to the 9th Evacuation Hospital while it was functioning in Germany during April and May of 1945.

#### CASE REPORTS

##### AMERICAN SOLDIERS

**Case 1—J. E. K.** This patient received a perforating rifle wound at 11 A.M. on April 3, 1945. Admitted on April 3, 1945. The wound of entrance was in the left inguinal region and the wound of exit in the left buttock. The abdomen was soft and there was no evidence of rectal injury or injury to the femoral vessels. X-ray revealed an extensive comminuted fracture of the left ilium involving the acetabulum.

## JOINT WOUNDS

The patient was treated for shock. He was brought to operation at 3 45 P.M., April 4, 1945, almost 29 hours after injury. Pulse 100. Operator J. E. T.

*Pathology* The wound of entrance was just medial to the anterior superior iliac spine. The bullet had entered the abdominal wall and had passed extra-peritoneally to pierce the ilium, shattering it into one large fragment and several smaller ones. It traversed the superior lip of acetabulum in its path, unroofing the joint. In emerging from the ilium it destroyed the gluteus minimus and maximus over a diameter of about 3 inches, leaving a large defect. The superior gluteal vessels had been completely divided. There were many small loose bone fragments, but no debris, just old blood clots.



FIG. 1-B —A spot film of left hip in Case 1. The hip-joint shows extensive arthritic changes and is painful, but there is 25 degrees of flexion.

*Procedure* Using a Smith-Peterson incision, the antero-superior aspect of the joint was exposed. The above pathology was outlined. The capsule of the joint was opened by means of a "Y"-shaped incision. The head of femur was examined and found to be uninjured. The joint was then thoroughly irrigated with warm saline, and closed with interrupted chromic gut sutures. The defect in the joint where the superior lip of the acetabulum had been destroyed, could not be closed by a muscle flap of gluteus minimus. This muscle was completely lacking in blood supply and had to be removed in its major part. The severed superior gluteal vessels were ligated. The wound was thoroughly



irrigated and 10,000 units of penicillin were instilled into the hip joint. Closure was performed by re-attaching the gluteus medius to the iliac crest, and suturing the overlying skin with interrupted fine wire sutures. The vertical portion of the Smith-Peterson incision was not sutured.

The wound of entrance was incised down to fascia, and a local debridement was performed. The wound of exit was located in the left buttock four inches from the midline and on a level with the greater sciatic notch. It was enlarged laterally revealing a large defect of gluteus maximus that communicated directly with the space left by excising the gluteus minimus muscle. It was impossible to obliterate the cavity. The wounds were left open, dry fine mesh gauze was applied to the raw surfaces. No drains. A plaster hip spica was applied.

*Follow-up* Secondary closure was performed in England, in April 1945. He was evacuated to the United States on June 1, 1945, with his wounds healed and in a double hip spica which was removed during June 1945. He wore a brace and was ambulatory from July 1, 1945. The brace was discarded in February 1946. He was discharged from the Army on December 10, 1946.

He was examined by one of us (J. E. T.) on January 16, 1947. He is now gainfully employed at a desk job. His main complaints are pain in the hip, and to a less extent pain in the left knee and left flank. He uses a cane and walks with a definite limp.

On examination all his wounds are found to be cleanly healed. There is  $\frac{3}{4}$ " measured shortening on the left side, in measuring from the umbilicus to the medial malleolus. When measuring from the anterior superior iliac spine the left leg measures the same as the right. The shortening is due to the upward shift of the fractured ilium and acetabulum.

The motion at the hip is limited to 20 degrees flexion, 5 degrees extension, 5 degrees internal rotation, and 5 degrees external rotation. The extension at the knee-joint is complete, and he can flex the knee to 90 degrees. There was marked atrophy of the left thigh and left buttock, there was only slight atrophy of the left calf.

X-ray examination of the pelvis to include the left hip reveals extensive healed comminuted fractures of the left ilium which involves the acetabulum. Definite encroachment on the pelvis is shown by the medially displaced acetabulum and pubic fragments. There is upward displacement of the acetabulum, plus cartilage absorption of the articulating surface of both the head of the femur and the acetabulum (Fig. 1).

*Comment*—This case illustrates a very severe type of penetrating wound of the left thigh, where a comminuted fracture of the ilium communicated with the hip-joint. The damage to the gluteal muscles was extensive, including early ischemic necrosis of the gluteus minimus due to destruction of its blood supply. Debridement of this wound could never have been accomplished as easily or as completely through any other type of incision. It is felt that if this patient had been given the usual conservative treatment with wound debridements, he would have been an excellent candidate for deep wound infection and secondary suppurative arthritis.

Functionally his result is poor, and he may come to hip fusion to control pain. On the basis of World War I experience he may well have been included in the 60 per cent mortality group.

**Case 2**—H. H. S. The patient received a bullet wound of left upper thigh on April 9, 1945. He was admitted six hours later. X-rays revealed a comminuted fracture of the neck of femur and greater trochanter. He came to operation 22½ hours after injury. Operator J. E. T.

*Pathology*—The wound of entrance was situated on the antero-lateral aspect of middle third of left thigh. In coursing upwards the bullet traversed the base of the neck of left

femur to lie, finally, just beneath the skin of left buttock about three inches lateral to the anus. The greater trochanter was also comminuted. In its course it destroyed about two-thirds of the tensor fascia muscle, and locally destroyed portions of the deep surface of the gluteus maximus muscle. The fracture lines extended into the joint proper.

*Procedure*—Smith-Peterson incision employed with the wound of entrance included in the vertical portion of the incision. The devitalized tensor muscle and the destroyed portions of the gluteal muscles were excised. Some clothing and bits of steel jacket from the bullet were also removed. The capsule of the joint was opened through a Y-shaped incision on its anterosuperior aspect and the fracture was seen to communicate with the joint. Actually the bullet had traversed the trochanter at an extra-capsular point.

The joint was irrigated with warm saline, and the capsule closed with a lock stitch of continuous chromic gut. 10,000 units of penicillin were injected into the joint. The bullet was then excised from beneath the skin of the buttock.

A postero-lateral incision, splitting the fibers of gluteus maximus, was made, and a rubber tube drain inserted to a point just posterior to the fracture line. (To be removed in three days.)

The Smith-Peterson incision was closed in layers, except for the distal half of its vertical portion.

The hip was reduced by the Ledbetter maneuver and a plaster hip spica was applied.

*Follow-up*—A letter received from patient on December 8, 1946, is as follows:

"I received your letter asking me about my hip wound. Well it sure turned out better than I ever thought it would. You asked me a few questions in your letter, I'll do my best to answer them.

"The first thing, my hip is healed and well. After I was operated on in the 112 Gen'l, I was put in traction. Ten days after they operated, the wound was well healed, but the bone itself would not knit. I was in traction 10 weeks and sent back to the States, here I was put in skin traction for three weeks, then up on a full leg brace, which wasn't so good. I was sent to Percy Jones Hospital after that, oh yes, this brace was gotten at Winter Gen'l Hospital in Kansas. After one month at Percy Jones they operated again and put in a steel plate which turned out all right so far.

"As for working I haven't done anything yet. I tried a few things back here on my Dad's farm but that's out. My leg is an inch short and throws me off balance to carry anything. So I have to look for some other sort of a job. My knee has only 90 degree bend and hip partially stiff.

"I am home now on Terminal leave, which is up the 15th of December, far as disability pension I wouldn't know as yet."

*Comment*—This case illustrates a bullet wound causing a severe compound fracture of the greater trochanter of femur, and the fracture line extending into the joint. The deep-seated destruction of muscle, and the clothing carried into the depths of the wound would have been difficult to discover with a simple type of incision. Suppuration of the hip joint would have been a likely complication following the conservative form of treatment.

**Case 3—D P** This patient received a shell fragment wound of the upper left thigh on April 19, 1945. He was admitted and operated on the same day. Operator J E T.

*Pathology*—X-ray had shown two large shell fragments adjoining the hip, one of which looked as though it might have penetrated the capsule. Actually one fragment was found lying on the antero-superior aspect of the capsule but had not penetrated it. The other one was found medially beneath the sartorius muscle.

*Treatment*—Smith-Peterson incision. The shell fragments were removed and the destroyed muscle tissue debrided. The joint capsule was not opened. The Smith-Peterson incision was closed except for the distal half of its vertical portion. A hip spica was applied.

*Follow-up*—A letter received from the patient's father on Dec 5, 1946, states that the patient underwent no further surgery. He was discharged from the Army and is now attending school. His hip is said to have 20 per cent limitation of motion.

*Comment*—This case was subjected to more surgery than was needed. The capsule of the joint was contused and not penetrated. It is inevitable that a certain per cent of negative explorations will occur.

**Case 4**—T A M. This patient received a bullet wound of the right anterior thigh on April 23, 1945, at 5 30 A M. *Primary operation* on April 24, 1945, at 2 30 A M. 21 hours after injury. Operator C F Stewart.

*Pathology*—A simple debridement of the wound of entrance was made and the tract was explored. The entrance was just lateral to the femoral vessels on the anterior thigh, and an x-ray had shown the bullet at the level of the neck of femur. It was thought that it was lying anterior to the capsule just below the sartorius muscle. A vertical counter incision was made between the sartorius and the tensor fascia muscles. At the end of two hours of search the procedure was abandoned. The wounds were left open and dry dressings were applied.

*Course*—On April 25, 1945, check-up x-rays, which included a lateral view, suggested that the bullet had penetrated the joint capsule, and was lying against the neck of femur.

*Secondary Operation* on April 25, 1945, at 3 P M. Operators C F Stewart and J E Thompson. The original counter-incision was extended upwards and converted into a Smith-Peterson approach. The antero-superior aspect of the joint was exposed. The capsule was opened with a V incision on its anterior surface, and the joint filled with 5 to 10 cc of bloody fluid. On the anterior surface of the head was a minor crushing injury to the cartilage, not sufficient to require debridement. The bullet was then found embedded within the substance of Bigelow's ligament opposite the superior surface of the femoral neck. It was partially within the joint. The bullet was removed and the openings in the capsule were closed with a continuous lock-stitch of chromic gut after irrigating the joint with warm saline. 10,000 units of penicillin were instilled into the joint.

The wound was then closed in layers except for the vertical portion of the Smith-Peterson incision which was not sutured. A hip-spica was applied.

*Follow-up*—A letter was received from this patient on Jan 15, 1947. He was still in the army as of that date. He states that his only subsequent operation was for secondary closure of his wounds. He is now suffering from slight stiffness at his hip-joint, with occasional pain in the hip and back.

*Comment*—This case beautifully illustrates the problems of penetrating hip-joint wounds as encountered and treated in the past. It emphasizes the time consumed in trying to trace the path of a foreign body which has penetrated deep into the tissues around the hip-joint. It shows the inadequacy of using an ordinary debridement incision to give the proper exposure. The knowledge gained by the preceding cases was of great help in deciding that a secondary operation was necessary, particularly after the x-rays were reviewed and new ones were obtained.

**Case 5**—S D S. This patient received a bullet wound of the left thigh on April 24, 1945, at 11 45 P M. The wound of entrance was on the antero-lateral aspect of the left thigh in the upper third. X-ray showed a fragmented bullet which seemed to be in the hip-joint.

Operation was performed on April 25, 1945. Operators G Crawford, J E Thompson

## JOINT WOUNDS

It was decided to approach this case using only the vertical portion of the Smith-Peterson incision, as the bullet was seen by x-ray at a point just anterior and inferior to the neck of femur. The incision was made to pass through the wound of entrance, and extended deeply between the sartorius and rectus femoris on the medial side and the tensor muscle laterally. The capsule of the joint was exposed and incised in the line of its fibers. The bullet fragments were removed both from the capsule and curetted from the substance of the neck of femur.

The joint was irrigated with warm saline, and snugly closed. 10,000 units of penicillin were instilled into the joint. The upper half of the incision was closed and the remainder left open. A hip spica was applied.

*Follow-up*—A letter from the patient on December 12, 1946, stated that his wound was sensitive but completely healed. He has occasional pain and stiffness of the hip-joint, particularly when he walks or stands too much. Upon his discharge from the Army he was allowed 30 per cent disability. He now has an easy civil service job.

*Comment*—The exposure using this type of incision was quite difficult in that it required considerable heavy retraction and only a limited view of the anterior part of the capsule. The many arterial branches entering the tensor muscle in its distal half added to the difficulty. The operation would have been easier, and the exposure improved by detaching the origin of the tensor muscle from the anterior superior spine and the infra-spinous portion of the crest of the ileum. This modification of the Smith-Peterson incision would be perfectly adequate to approach the antero-inferior portion of the hip-joint.

**Case 6—N M** This patient received a bullet wound of the left buttock on May 4, 1945, at 9 30 P M and was admitted on May 5, 1945. X-ray revealed the bullet adjoining the neck of femur on its posterior aspect. Operation at 5 A M on May 6, 1945, 32 hours after injury. Operator: G Crawford.

A posterior approach was utilized as described by Langenbeck, passing through the wound of entrance. The fibers of the gluteus maximus were split, and the gluteus medius retracted anteriorly. The bullet passed through the piriformis muscle to enter the joint. The capsule was incised and the bullet removed. A small fractured area of the rim of the head of femur was debrided and the joint was irrigated with warm saline. The capsule was closed and 10,000 units of penicillin were instilled into the joint.

The soft tissues were not sutured. A hip spica was applied.

*Follow-up*—The only information that could be obtained about this patient was that he was back at regular duties with the Army of Occupation in Europe in February, 1946. This fact would indicate that his disability was minimal.

*Comment*—This case illustrates the adequacy of the posterior approach for selected cases where the pathology is limited to the posterior aspect of the joint. It is a much less destructive incision.

### GERMAN PRISONERS

(No Follow-Up Obtainable)

**Case 7.—E S** The patient received a perforating bullet wound of left thigh at 4 P M April 5, 1945. He was admitted at 1 A M April 6, 1945. Examination revealed a wound of entrance just below and medial to the left anterior superior iliac spine, the wound of exit was in mid-left buttock. There were other irrelevant wounds. The clinical signs pointed definitely to joint involvement.

*Operation*—April 6, 1945, at 2 20 P M 22½ hours after injury. Operator: J E T

*Pathology*—The bullet had traversed the thigh and buttock just superior to the capsule. No penetration of the capsule could be found. The gluteal muscles were quite healthy looking and only a moderate amount of debridement was necessary.

*Procedure*—Smith-Peterson incision. The capsule was opened with a V-incision, the joint was inspected and found to be negative. Several small fragments from the bullet were removed from the soft tissues outside the capsule. The capsule was snugly closed with a running lockstitch of chromic gut. Penicillin 5000 units were instilled in the joint. The incision was closed in layers except around the wounds of entrance and exit. A hip spica was applied.

*Comment*—This case had no actual penetration of the hip-joint in spite of the clinical signs, which were probably due to contusion of the capsule. There was very little deep destruction of soft tissues, so that the end result will not be materially benefitted by the Smith-Peterson incision.

**Case 8**—K. G. The patient was admitted on April 11, 1945, with a penetrating bullet wound of the left buttock. An A. P. x-ray view was taken and the bullet was interpreted as lying in the soft tissues of the buttock.

*Operation*—April 11, 1945. Operators: K. E. Black and T. Healy.

*First Procedure*—A transverse incision was made through the wound of entrance in the line of left buttock crease. Considerable time was spent in an unsuccessful effort to find the bullet, only a gutter fracture in the outer table of ilium was discovered. Further operation was abandoned.

Postoperative x-rays were taken on April 12th and 13th. A lateral view taken on the latter date gave fairly definite evidence that the bullet was imbedded either in the capsule or in the joint itself.

*Second Procedure*—April 13, 1945. Operators: J. E. Thompson and K. E. Black.

*Procedure*—Smith-Peterson incision. The anterior and superior surfaces of the capsule showed no evidence of penetration or trauma. The bullet could not be seen or felt. A bi-manual examination with a finger in each of the anterior operative and posterior wound of entrance revealed that the bullet, after creasing the outer table of ilium, had entered the base of acetabulum at about 7 o'clock (in the recumbent position).

The capsule of the joint was incised from the base of neck to acetabular rim along its superior surface, and then converted into a Y by an additional incision posteriorly inclined to get sufficient exposure. The base of the bullet was exposed, lying partly in capsule and partly in the joint. It was separated and cushioned from the femoral head by the "Labrum Glenoidal," in whose substance it was also imbedded, and which it had partially divided at one point along its periphery. The bullet was removed and two small clots evacuated, no further evidence of joint damage could be detected.

The capsule was closed with a continuous lock-stitch of chromic gut. The Smith-Peterson incision was completely closed in layers, relying on the posterior wound for drainage. A hip spica was applied.

*Comment*—This case illustrates joint involvement can be missed, particularly where x-rays are misinterpreted or the views are not satisfactory. The Smith-Peterson incision distinctly facilitated the location and removal of the bullet. Suppuration would very likely have developed, as one of the complications, if conservative treatment had been followed.

**Case 9**—L. N. The patient was admitted at 3:20 A. M. on April 23, 1945, with a gun shot wound of the buttock. X-ray examination showed the bullet lying within the neck of femur at the level of the capsule attachment near the posterior cortex.

*Operation*—April 23, 1945. Operators: G. Crawford and J. E. Thompson.

JOINT WOUNDS

*Pathology*—The bullet entered the left lower buttock 8 cm from the midline, and pierced the hip joint through the superior gemellus 1 cm lateral to the rim of the glenoid. It penetrated the head of the femur through a small round hole and passed down the neck of femur just beneath the cortex.

*Procedure*—Incision was the postero-lateral approach of Langenbeck. The gluteus maximus tendon was partially incised near the trochanter and the incision extended toward the postero-superior iliac spine splitting the muscle fibers. The origin of gluteus medius was slightly freed from the trochanter and the muscle retracted anteriorly. The joint capsule was exposed and opened inferior to the piriformis muscle. It was opened with a right-angled incision. The bullet was removed by unroofing the tunnel in the head and neck of femur.

The joint was lavaged with warm saline, and closed with a continuous lockstitch of chromic gut. 10,000 units of penicillin were placed in the joint. The exploratory wound was closed in layers. The wound of entrance was debrided and left wide open. A plaster hip spica was applied.

*Comment*—This posterior approach of Langenbeck gave beautiful exposure after the origin of gluteus medius was partially detached. The best exposure of the head was obtained posterior to the piriformis, instead of anterior to it as described by Langenbeck.

SUMMARY

A penetrating wound of a joint, aside from its destructive effect on the joint mechanism, is likely to result in suppuration unless the utmost care is exerted towards its prevention. This sequence of events occurs in any joint, large or small and seems to have a direct bearing on the delicate blood supply to the cartilaginous surfaces of the joint. A wound that combines the destruction of cartilage with the introduction of foreign debris is even more likely to develop this unfortunate complication.

Suppuration involving the hip or knee-joint at times is attended with such severe sepsis that life is threatened. The same threat to life is rarely seen following suppuration of the other major joints such as the shoulder, elbow, wrist and ankle, but the same principles of prevention and treatment of these joint wounds should be followed.

Warfare presents the opportunity to see joint wounds in sufficient numbers and variety to permit an organized surgical attack on the problem, in an effort to reduce the morbidity and mortality.

TABLE I  
PENETRATING WOUNDS OF KNEE-JOINTS

Source	Era	Number of Cases	Suppuration	Amputation	Mortality
British Army	1914	?	Nearly all cases	60-80%	?
	1916	?	25%		15%
	1917	?	12%	7%	8%
U S Army (Pool)	1918	34	8.8%	?	?
U S Army (two evac hosps)	1945	227	0.9%*	0	0

\* These two cases were suppurating on arrival at the hospital. One injured 10 and the other 14 days prior to admission.

A glance at Table I reveals that in 1917 the mortality rate following knee-joint injuries had dropped to 8 per cent as reported by the British Army, while in 1918 the incidence of suppuration as reported by the U S Army Medical Dept was 88 per cent

Pool outlined in detail the treatment of penetrating wounds of the knee joint from his experience in World War I, and today it serves as a model. The principles of treatment which he advocated were employed by several Evacuation Hospitals in the U S Seventh Army during 1945. In reporting 227 penetrating knee-joint wounds, it is to be noted that only two cases developed suppuration. Although the follow-up is incomplete, none are known to have died or to have required amputation. In brief, the underlying principles of treatment are as follows: (1) Wide formal arthrotomy through the wound of entrance or exit if convenient, but the essential point is good exposure of the inside of the joint so that all devitalized bone and cartilage, debris and foreign bodies can be removed. (2) Copious irrigation of the joint with warm saline. (3) Separate debridement of the wound of entrance and exit. (4) Complete, water-tight closure of the joint capsule at all points. Where a defect of capsule exists, it must be closed by a sliding flap of skin or fascia, or even a free fascial graft if necessary. (5) The skin is left open to be closed secondarily on the 4th to 7th postoperative day. (6) If a compound fracture of the patella exists, the patella in most instances should be excised. (7) The only addition to the treatment as formerly outlined by Pool, was the local and systemic use of penicillin, and the emphasis on complete postoperative immobilization of the knee-joint by means of a hip spica instead of a high thigh cast.

TABLE II  
PENETRATING WOUNDS OF THE HIP JOINT

Source	Era	Number of Cases	Number of Cases Followed	Total Mortality
Langenbeck (Franco Prussian War)	1870-71	132	131	77.2%
Otis (Civil War)	1865	386		85%
British Army (World War I)	1914-18	?		60%
Madier (French Army)	1914-18	39	37	37%

A glance at Table II shows the high mortality attending hip joint wounds as seen in previous wars.

In World War II, hip-joint injuries continued to be a serious problem with appreciable numbers suppurating and developing profound sepsis. It became apparent that the surgical principles which had been applied so successfully to knee-joints were not being carried out for the hip. Its deep location made it difficult to approach, debridements were as a result usually incomplete, and inspection of the joint capsule was inevitably rare. In addition minimal injuries to the capsule, head, neck and femoral trochanter were often overlooked early after injury, because one's attention was not specifically focused on the joint itself.

In March 1945 it was suggested by the 7th Army Consultant that all suspected hip-joint wounds were to be submitted to a formal arthrotomy. The Smith-Peterson approach was to be used by preference, and where it was desirable to expose the joint posteriorly, the postero-lateral approach of Langenbeck was to be employed

We encountered nine penetrating hip-joint wounds during the month of April 1945. The pathologic findings were as follows

- |   |   |         |
|---|---|---------|
| a | Fractures involving ilium and acetabulum  | 2 cases |
| b | Fracture of the neck and greater trochanter of femur  | 1 case  |
| c | The capsule penetrated and the bullet found imbedded in capsule and partly within joint, with minimal damage to the head or neck of femur | 3 cases |
| d | Bullet lying completely imbedded in the neck of femur   | 1 case  |
| e | Simple contusion of the joint capsule   | 2 cases |

Six cases were American soldiers, and three were German prisoners of war. No follow-up has been obtainable on the Germans, but letters have recently been received from all the Americans. None of the six cases suppurated, none had to be amputated and there were no deaths. None have draining sinuses, the wounds being completely healed. Five out of the six complain of some pain and have some degree of limitation of motion. One of the most severe cases was personally seen and examined, he walks with a marked limp, has a moderate amount of pain and only about 25 per cent motion at the hip joint. X-ray examination shows an upward shift of acetabulum secondary to mal-union of a comminuted fracture of the ileum. There is also marked arthritic change about the joint (Fig. 1)

#### CONCLUSIONS

In conclusion it is thought that the complications of penetrating joint wounds will be reduced to a minimum by adhering to the following principles of treatment

- 1 Operation at the earliest possible moment after injury
- 2 Wide exposure of the joint, by means of a formal arthrotomy, in order that the capsule and inside of the joint can be thoroughly inspected
- 3 The joint should be irrigated with saline and completely cleansed of all devitalized bone, cartilage and foreign debris
- 4 The joint capsule must be closed "water-tight" at all points
- 5 Complete immobilization of the joint postoperatively.
- 6 Penicillin locally and systemically

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DISCUSSION—DR FRANK B BERRY, New York Six cases is not a large series, but I think six cases of wounds such as you saw in the last patient, all of which are thoroughly healed without having undergone sepsis, are noteworthy in wounds of the pelvis and hip joint I think this principle of debridement can be applied to civilian life More than 20 years ago when I was a junior on the staff, I opened a knee joint for a bullet wound with compound fracture, as described by Doctor Thompson, debrided it and sewed it up tight Twelve days later the patient had complete mobility of the joint I was impressed with this

Doctor Pool, who was with us, had a reprint of his father's to guide us, and when we were confronted with these cases we early established the principle of opening and debriding all wounds of the knee joint I talked it over with Doctors Taylor and Thompson, who are here, and with Doctor McNeil of the Sacramento Unit, and we decided that up to three days, if we were not able to do it at first, we would similarly perform formal arthrotomies in hip joint wounds, realizing that in wounds involving joints, if suppuration does not result immediately, there are certain natural defenses Hence, during the latter part of the war we elected to try this procedure Instead of sending patients back to face a period of sepsis, we sent them back with clean, even though damaged joints, which could be handled by the orthopedists in general hospitals, who could then proceed with these patients who were not septic

When we were in Naples we were detached from the American Army and assigned to the French This gave us six months to follow and study our patients as we were not obliged to evacuate our severely wounded We were confronted with six patients with suppurating knee joints We went around to our American friends but could not get any help on how to handle them, except to immobilize and amputate when necessary We did have to amputate in one instance to save life The French surgeons said, why not resect these joints? Inasmuch as the French did not supply prostheses, we were confronted with the necessity of choosing between amputees without prostheses, or joint resection and stiff leg, so we elected to resect these patients

(Slides) This boy was resected and sent back with his wound healed, with the thought that at least the leg was preserved, and that some future operation could be performed to strengthen the leg. We were confronted with these two problems, so we went back to resection as advocated many years ago, and considered it a worthwhile procedure and preferable to amputation.

DR GUY A. CALDWELL, New Orleans. This is a very excellent lesson in technic, worked out in military life, which should be carried into civilian life. Many small puncture wounds of the knee which look harmless at the time, too often result in joint suppuration, even when penicillin has been administered. Such wounds need exactly the same management that has been outlined by the speaker, viz., debridement, cleansing the joint, suture, immobilization and penicillin therapy.

DR I. RIDGEWAY TRIMBLE, Baltimore. The nature of residual pain is most interesting. I should like to ask if the incidence of causalgia was studied. A young man wounded in 1944 came under my care recently. He was struck in the ankle, with partial severance of the posterior tibial nerve, and was in the hospital for 19 months. He had so much pain that he came to the orthopedic surgeon for amputation. If he stubbed his toe he would cry with pain, scuffing his foot gave intense pain. He was submitted to a lumbar sympathectomy and has since been completely relieved of pain.

MAJOR GENERAL NORMAN T. KIRK, Washington, D. C. We should thank Doctor Berry and Doctor Thompson for this contribution. As was stated in their paper, Doctor Pool pointed out, in World War I, proper debridement of joints was essential if infection was to be prevented and this was made of record in the medical history of that war, yet during the peace that followed the war and when World War II came, the medical profession had not taken advantage of this information or had failed to read the literature which contained the answer. I hope that when we plan for the next war, or when it is imminent, someone will find and read this paper which has been presented here today.

Unfortunately, proper debridement was more often done in injuries to knee joints and other small joints than it was when the hip joint was involved. The proper debridement of a hip joint is a formidable operation and not too many surgeons are sufficiently trained to properly perform it. The hip joint lies deep in muscle structure and when involved in battle wounds is often complicated with visceral or multiple injuries or both.

If infection is to be prevented in joints, early proper debridement is essential. If this infection is not prevented the joint is destroyed and too often, in order to save a patient's life, a joint resection or an amputation is required. It is believed that the proper debridement of joints and compound injuries in civil life is as essential as it is in the Army.

DR CARL EGGERS, New York. I arise to call attention to another phase of the subject, that is, that this presentation illustrates the importance of basic training of surgeons. Doctor Berry is at present known principally for his work in thoracic surgery. When he was confronted with war surgery his mind reverted to his early training and experiences. This emphasizes the great importance of not encouraging too early specialization, but to give all surgeons training in general surgery before they embark on a specialty.

DR LEO ELOESSER, San Francisco. I would like to ask Doctors Berry and Thompson whether they closed the skin and soft parts, or left them open.

DR EDWARD D. CHURCHILL, Boston. The points raised by General Kirk and Doctor Eggers are very important. Military surgery is a discontinuous specialty and stops when the last shot is fired, then is forgotten. We knew too little of the surgical experience of World War I. I was a member of the N. R. C. Committee assigned to prepare a manual of war surgery. If the men assigned these tasks had gone back to the literature of

World War I and based their manuals on the writings of the surgeons who participated in that conflict, the results would have been more helpful

The second question brought up by Doctor Eggers—why did we have trouble getting these basic principles adopted by surgeons? Early in World War II we were dealing with specialists in civilian surgery, not with military surgeons. I personally pleaded with orthopedic surgeons to follow Doctor Berry's recommendation regarding the knee joint, but they thought it unsound to think of opening a knee joint in the operating tent of an Evacuation Hospital, quite forgetting that the dirt, torn uniform and devitalized cartilage within the joint was a far greater hazard than the tarpaulin flooring and other relatively crude provisions for aseptic surgery. It was impossible to convince the general surgeon that he should do a wide arthrotomy on a hip joint. He had never seen the operation and did not know the anatomy.

DR JAMES E. THOMPSON, New York (closing). I wish to thank all the discussors. In reply to Doctor Trimble's question about causalgia, I think it is an interesting possibility as a cause of the pain. We have had no experience in treating such cases with sympathectomy. In the one case on which we were able to obtain a check-up x-ray examination there is a lot of arthritic reaction about the hip joint, which must be the cause of his pain. I would not be surprised if his hip joint has to be fused at a later date.

In answer to Doctor Eloesser, the skin was always left open, to be closed secondarily in a four- to seven-day period. We either closed them ourselves, or the closure was performed later at a general hospital.

# PULMONARY CAVERNOUS HEMANGIOMA WITH ARTERIO- VENOUS FISTULA, SURGICAL MANAGEMENT.

## CASE REPORT\*

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VISCERAL HEMANGIOMAS are uncommon. Autopsy records indicate an incidence less than 0.3 per cent. Hemangiomas of the lung are rare and for this reason I felt that my case should be added to the small group previously reported.

Hepburn and Dauphinee searched the literature to the time that they reported their case in 1942 and summarized their findings as follows, "Cavernous hemangioma of the lung is not mentioned in Henke and Lubarsch's Handbook of Pathology. This work, however, does refer to a case described by de Lange and de Vries-Robles (1923) of an infant age two and a half months, whose lungs, at autopsy, were seen to contain two small tumors, which microscopically were shown to be capillary hemangiomas. Wollstein in 1931 reported a malignant hemangioma of the lung which was found at autopsy in a child aged four months, and Hall in 1935, also described, a malignant pulmonary hemangioma in a woman aged 40. In both these malignant cases there was a distinct anemia and an appreciable lowering of the red blood count. Bowers, in 1936, reported the death of a new-born child caused by hemorrhage from a ruptured pulmonary angioma. In 1939, Duvoir et al. related the case of a child who, from 1932, had been subject to paroxysms of dyspnoea and who had congenital lues. Roentgen rays of the chest showed an opacity which was thought to be caused by a lipoma. Pathologic examination of the removed tumor, however, showed the mass in the lung to be a hemangioma. The child died of pneumonia five years later and autopsy revealed many lipomata, visceral angiomas and a lipoangioma. Cyanosis and clubbing of the fingers were not mentioned and no blood examination was recorded."

The review of Hepburn and Dauphinee included two additional cases, one reported by Rodes in 1938 and one by Smith and Horton in 1939. To these they added their case.

Rodes, it would seem, should be credited with the first description of pulmonary cavernous hemangioma as a clinical entity. In the eight years following his report ten additional cases have been recorded, including my case. Two deductions are evident, cases existing prior to 1938 were not recognized and second the lesion is not as rare as the above figure suggests.

Smith and Horton, accredited with having made the first ante mortem diagnosis, pointed out a characteristic clinical syndrome and its physiologic basis. And from the additional contributions from the case studies of Hepburn and Dauphinee, Goldman, Janes, Jones and Thompson, Adams, Thornton and

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Eichelberger, Shenstone and Makler and Zion a comprehensive picture of the entity and its pathologic and clinical variations has evolved

The hemangiomas in most instances have been unilateral and near the hilus but in the cases reported by Rodes and Makler and Zion and in one of Janes' cases there were multiple hemangiomas involving both lungs

How these lesions should be classified is of academic interest principally Anatomically, they are hemangiomas, physiologically antero-venous fistulas As a matter of fact, Reid, Horton and others are of the opinion that all hemangiomas are abnormal arteriovenous communications through which arterial blood flows from arteries to veins without passing through a capillary bed

Probably all pulmonary hemangiomas are congenital Their presence has been demonstrated in newborn infants and in some of the reported cases there has been a history of cyanosis since infancy Why symptoms do not appear until later in life in some cases may be explained by the fact that cyanosis and symptoms associated with it result from a large shunt of blood from the pulmonary artery to the pulmonary veins It has been estimated that at least 25 per cent of the blood must be shunted before cyanosis is apparent It would seem reasonable to assume that a small fistula through a hemangioma would progressively enlarge to a size that would produce symptoms as time passed There is no record of a pulmonary arterio-venous fistula of traumatic origin and, furthermore, in the reported cases there is no definite evidence of an etiologic factor other than a congenital one

In terms of oxygen saturation the direction of blood flow through a fistula in the lung is the reverse of that through a shunt in the systemic circulation Therefore, much of the blood leaving the left ventricle is venous and unsaturated with oxygen so that some degree of cyanosis is a constant symptom The cyanosis is somewhat distinctive in that there is no associated enlargement of the heart or other evidence of a cardiac lesion but there is, with exceptions, a compensatory polycythemia, polyemia and hyperhemoglobinemia with an increased hematocrit and reduced oxygen saturation The degree of cyanosis and polycythemia is dependent upon the size of the fistula and the volume of the shunt and the increase in the number of red cells accounts for the increased blood volume, there being no appreciable increase in serum and none in the number of white blood cells and platelets The blood picture differs also from that of true polycythemia by absence of changes, such as basophilic stippling and immaturity of the white cells A constant finding is the presence of one or more chronic non-progressive pulmonary lesions which roentgenographically are cylindrical masses and which under the fluoroscope often may be observed to pulsate In laminagrams the cylindrical configuration and branching character of the lesions may be demonstrated

In five of the reported cases and in my case a continuous murmur was heard over the pulmonary lesion and in each instance it was loudest at the end of deep inspiration

Clubbing of the fingers and toes is a constant finding The extent of these changes varies with the duration and the degree of cyanosis

Other symptoms are variable including pain in the chest, cough, dyspnoea, asthmatic paroxysms, hemoptysis, fatigue, vertigo, faintness, headaches, syncope and disturbances of speech and vision

Treatment consists of ablation of the fistula. This can be accomplished only by surgical interference. Operation is indicated in the absence of incapacity and even in the absence of noteworthy symptoms because of risk of fatal hemorrhage from rupture of the hemangioma and of sequelae resulting from thromboses secondary to the polycythemia.

Seven cases including mine have been operated upon and all have been cured. In four, (Shenstone and Janes, one, Jones et al, one, Adams et al, one and Goldman's case) a total pneumonectomy was done, in two, including my case a lobectomy and in one, a case of Janes, local excision of multiple bilateral lesions. The ideal operation would eradicate the hemangioma by interrupting the vessels communicating with it without sacrificing pulmonary tissue. Unfortunately, this has been technically impossible except in Janes' case.

#### REPORTED CASES

In 1938 Rodes reported a 25-year-old male with a history of cyanosis and dyspnoea as long as he could remember and clubbing of the fingers since the age of 15. His heart was normal and there was no congenital defect. He died of a massive hemorrhage from a ruptured hemangioma. His red blood cell count was 7,540,000 and the hemoglobin 118 per cent. A roentgenogram showed spherical shadows in both lower lung fields. Postmortem examination revealed hemangiomas both lower lobes, two in the right and one in the left.

The second case and the first one diagnosed ante mortem was reported in 1939 by Horton and Smith. Their patient, a male of 47 years, stated that he had been a "blue" baby at birth and had been aware of cyanosis and of clubbing of the toes and fingers since the age of 24. When first examined by Horton and Smith in 1932, there was in addition to the cyanosis and clubbing a polycythemia, a red cell count of 6,000,000 and a hemoglobin of 20.6 Gm leading to a diagnosis of polycythemia vera. When re-examined six years later a continuous murmur was heard at the base of the right lung. A roentgenogram of the chest showed a shadow of increased density in the right posterolateral lung field. This was demonstrated to be a vascular tumor by injection of radiopaque solution into the basilic vein.

Hepburn and Dauphinee in 1942 reported the third case and the first one cured by operation. This patient, a female of 23, complained of dyspnoea, attacks of dizziness, faintness and thickness of speech, cyanosis and clubbing of fingers and toes. The red blood cell count was 9,600,000, hemoglobin 140 per cent, and total blood volume 8,500 cc. Oxygen saturation of the arterial blood was 70 per cent. An X-ray film of the chest revealed a shadow in the right middle and lower lobes. No bruit was heard over this area. A right total pneumonectomy was done by Shenstone and Janes and a cavernous angioma was demonstrated in the resected lung. There was a rapid and complete relief of symptoms and signs.

Goldman in 1943 reported a man of 22 who had had slight cyanosis since infancy. For seven years there had been increasing cyanosis, dyspnoea and frontal headaches and at the time of admission the additional complaints of weakness, nausea and vomiting. The red blood count was 11,450,000, the hemoglobin 137 per cent, oxygen saturation of the arterial blood 70 per cent, blood volume 8,170 cc and plasma volume 2,450 cc. A dense shadow in the left lung field was demonstrated by means of laminagrams and a kymiogram to be a solid branching mass with an intrinsic pulsation which was synchronous with that of the pulmonary artery.

Treatment with roentgen rays, radioactive phosphorous and venesection was ineffective. A total pneumonectomy resulted in complete relief of symptoms.

Recently Goldman reported that his patient has a brother, 32 years of age with the same but less severe clinical picture.

Janes in 1944 reported a man, 30 years of age who had coughed up bright blood on several occasions over a period of two years. His lips and fingernails were definitely cyanotic and there were multiple small hemangiomas on the lower lip. A soft blowing murmur was heard in the region of the right cardio-phrenic angle. Radiographs of the chest showed two shadows in the right lung and one, or possibly two, in the left. There was no polycythemia.

The hemangiomas in both lungs were subpleural and were locally excised. The right side was operated upon first and two separate lesions removed, one by individual ligation of the vessels entering the hemangioma and the other by resection between clamps. Six months later the two lesions in the left lower lobe were excised. He recovered without incident.

In discussion of a paper by Jones and Thompson (abstracted below), Janes mentioned another case upon whom Shenstone and Janes performed a lobectomy for a hemangioma with cyanosis but no polycythemia.

In 1944 Adams et al reported a man 24 years old complaining of frequent nosebleeds and colds for three years and of a cyanosis and of clubbing of the fingers and toes for at least 16 years. Examination revealed extreme cyanosis, marked clubbing of fingers and toes and several small hemangiomas of the lip and face. The red blood count was 7,200,000, the hemoglobin 23.0 Gm, the hematocrit 82 per cent, the vital capacity 3,800 cc, the total blood volume 12,750 cc, the plasma volume 2,420 cc and the oxygen saturation of the arterial blood 71 per cent. Roentgenograms of the chest showed a lobulated moderately opaque area measuring 25 sq cms between the 7th and 9th rib posteriorly in the left lung and a second similar but smaller opacity in the right lung.

A left total pneumonectomy was done. Convalescence was uneventful and there was rapid restoration of normal blood volume, red blood cell count and oxygen saturation of the arterial blood and disappearance of cyanosis and other symptoms.

Jones in 1944 reported a woman aged 24 years. She had been very cyanotic since birth and had had increasing clubbing of the fingers since nine years of

age Examination revealed in addition to the cyanosis and the clubbing of finger and toes, a loud, rough roaring murmur probably continuous and loudest at the end of inspiration over and just beneath the right breast

Roentgen studies including planigrams showed an 8 or 10 cm rounded area of increased density in the right lower lung field with communicating masses interpreted as dilated branches of the pulmonary artery Fluoroscopically the whole thing seemed to pulsate The mass at one area appeared calcified The red cell count was 7,080,000, hemoglobin 130 per cent, plasma volume normal and whole blood volume 170 per cent

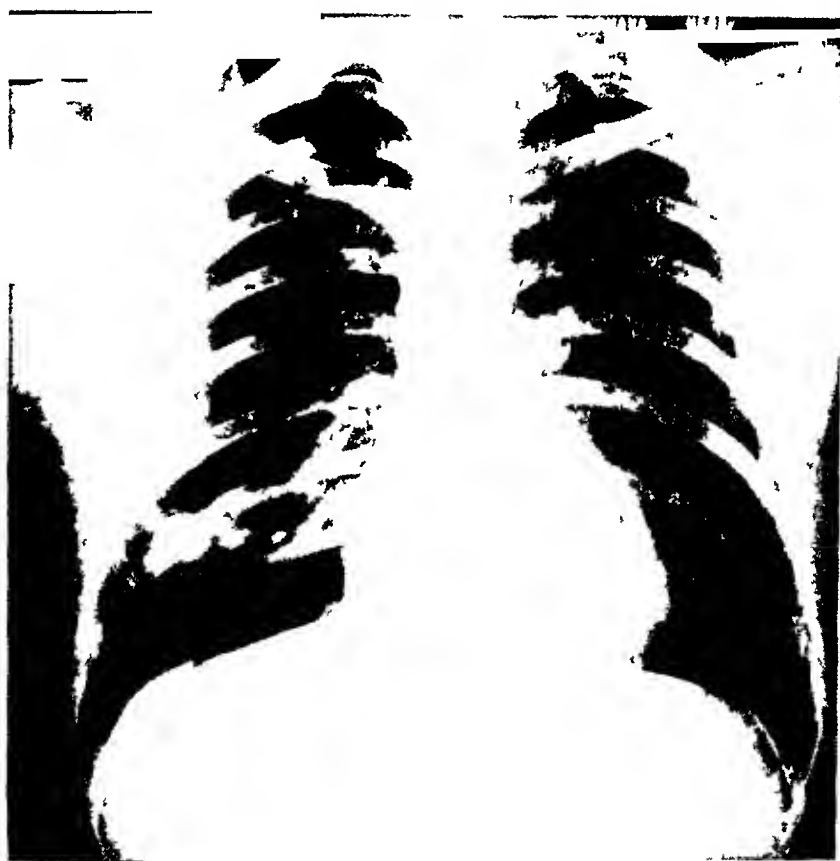


FIG 1—3 x 4 cms ovoid shadow of increased density in the lower right lung field at the level of the 9th rib and 11 cms from the midline In lateral view it was posterior Note two tortuous linear shadows extending from the mass toward the hilus These are no doubt dilated pulmonary vessels

A right total pneumonectomy was followed by immediate disappearance of cyanosis and a prompt return of the blood to normal and a cure

In 1946 Makler and Zion reported a man 20 years of age with a history of marked cyanosis, slight dyspnoea and occasional headaches and nosebleeds for three years. Examination revealed telangiectasis behind the right ear, cyanosis and clubbing of the fingers and toes The red cell count was 7,700,000 and the hemoglobin 19.5 Gm Roentgenograms showed four rounded shadows, three in the right lower and mid-lung fields and one in the left mid-lung field The



Valsalva experiment was positive and laminagrams showed a worm-like configuration of the masses and a continuation of these masses with linear shadows from the hilus

The patient had insufficient incapacity to desire and warrant operation

#### CASE REPORT

A railroad switchman of 29 was admitted to the Union Pacific Department of Saint Joseph's Hospital, July 17, 1946. He had pneumonia eight years ago and since then progressive dyspnoea on exertion, nocturnal asthmatic attacks and a dry cough. He had

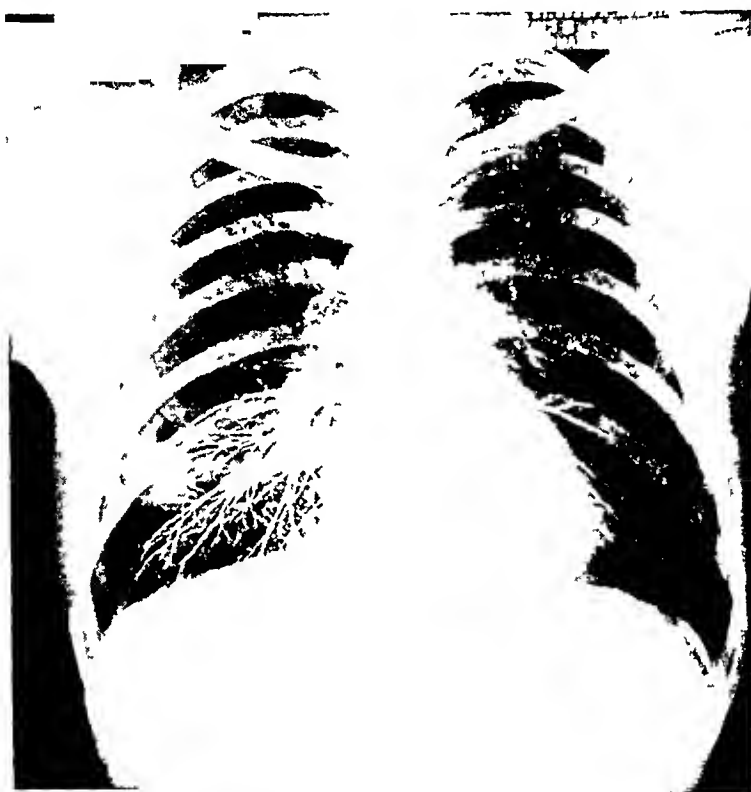


FIG 2—This bronchogram places the shadow in the lower lobe and indicates that there is no association to the bronchial tree

been aware of cyanosis of his lips and fingernails for six years. During the last three years he had several attacks of loss of consciousness which lasted only a few minutes, frequent headaches and episodes of blurring of vision, and chronic fatigue. For one year there had been a dull pain along the right sternal border and for three months he had been unable to work on account of fatigue and breathlessness on exertion.

The positive findings in the physical examination were: Moderate cyanosis, slight clubbing of fingers and toes, multiple small blue hemangiomas of lips, dyspnoea from climbing half a flight of steps, a vital capacity of 2,800 cc, a rough continuous murmur over the lesion under the right eighth rib in the posterior axillary line, louder on inspiration and a blood pressure of 95/65 in both arms. Blood studies revealed a hemoglobin of 18 grams, red blood cells, 6,800,000, white blood cells 8,300 with a normal differential and a hematocrit of 71 per cent. Blood volume and its oxygen volume and tension were not determined. The electrocardiogram was normal.

The roentgenologic report was as follows: There is a sharply delineated ovoid nodular shadow of increased density measuring 3 x 4 cms, lying well posterior and 11 cms to the right of the midline at the level of the 9th rib in the posterior axillary line. Bronchograms of both lower lung fields show no evidence of bronchiectatic change and no communication between the nodular lesion and the bronchial tree (See Figs I and II). A diagnosis of arteriovenous fistula of the right lower lobe was made. Under intratracheal cyclopropane anesthesia and through the 7th intercostal space the right pleural cavity was opened. There were no pleural adhesions and the interlobar fissure was well defined but there was no middle lobe. Throughout the entire lower lobe there was a thrill which disappeared upon digital compression of the vessels to the lower lobe near the hilus and over the lobe at the point of maximum intensity of the thrill. The lower lobe was removed by dissection and individual ligation technique. The upper lobe was expanded and expansion maintained with constant suction through two air-tight catheters. Chemotherapy started 24 hours preoperatively was continued for five days. Blood was not given. Oxygen was administered for 24 hours. The patient made an uneventful convalescence and has remained free of symptoms. Examination, two and one half months after operation, revealed no cyanosis, a hemoglobin of 13.5 Gm, a red blood count of 4,200,000, white blood cells 6,800 with normal differential and a hematocrit of 53 per cent. The vital capacity was 3,200 cc.

The resected lobe was injected with a barium mixture through a cannula in the pulmonary artery. The mixture returned freely through the pulmonary veins. A roentgenogram of the injected specimen appears in Figure III.

Dissection of the lobe revealed two cavernous hemangiomas measuring 2 x 4 cms and 1 x 2 cms. Vessels communicating with these spaces were not demonstrated.



FIG 3—Roentgenogram of the excised right lower lobe after injection of a thin aqueous barium suspension into the pulmonary artery through the left upper cannula. The other two are in pulmonary veins and are filled with the suspension as is the distended hemangioma, demonstrating the shunt. The incomplete filling of ramification of the pulmonary artery indicates that passage through the fistula is the way of least resistance and the course which was followed by most of the blood passing through that lobe.

#### CONCLUSIONS

- 1 Cavernous hemangioma of the lung is a relatively rare lesion but not as rare as the number of reported cases suggests.
- 2 It is probably a congenital lesion and may exist without symptoms until an arteriovenous shunt becomes established or of such a size as to cause con-

siderable reduction in the oxygen saturation of the arterial blood. There is then a characteristic syndrome, a demonstrable pulmonary lesion which may be demonstrated to have characteristics of a vascular tumor by roentgenographic studies and an associated generalized cyanosis with clubbing of the fingers and toes. In most cases, but not invariably so, there is a compensatory polycythemia.

3 Treatment consists of ablation of the vascular fistula. Ideally this should be accomplished without sacrificing pulmonary tissue as has been done in one case. Usually this is technically impossible and eradication can be accomplished only by means of a lobectomy or pneumonectomy. Since there is much hazard of a fatal hemorrhage or of thrombotic sequelae from an associated polycythemia, surgical interference is indicated in the absence of incapacity and even in the absence of troublesome symptoms if there are no additional factors to increase seriously the risk.

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# CONTROL OF HEMORRHAGE FROM WOUNDS OF THE HEART BY THE GELATIN SPONGE "PATCH" TECHNIC\*†

A New Experimental Method

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IN SEVERAL PREVIOUS COMMUNICATIONS, the absorption<sup>1</sup> and hemostatic action of gelatin sponge have been presented. In a series of 30 experiments on dogs, the bleeding from wounds of the liver, kidneys, and spleen was controlled by the gelatin sponge.<sup>2</sup> In another series of 12 experiments, a lobe of the liver was resected and the hemorrhage controlled by a "blanket" of gelatin sponge applied over the resected stump.<sup>3</sup> In 36 experiments on dogs, wounds were made in veins of which 28 were in the vena cava.<sup>3</sup> The bleeding was stopped by a "patch" of gelatin sponge except in two experiments where the animals died of uncontrolled hemorrhage at the time of operation and in one experiment where there was secondary hemorrhage. In a series of 17 experiments where wounds were made in the aorta of dogs, the bleeding was controlled by a cuff of gelatin sponge wrapped about the vessel and supported by a sheath of chromic catgut.<sup>4</sup> These experiments were performed for the most part without the addition of thrombin to the gelatin sponge and without any supplementary suturing. In view of the satisfactory results which were generally obtained in these experiments, the possibility of using the gelatin sponge by the "patch" technique for wounds of the heart naturally suggested itself. A preliminary report of this technique has been made.<sup>5</sup>

## EXPERIMENT

The dogs were anesthetized with ether and an intra-tracheal tube inserted. The anesthesia was maintained during the operation with positive pressure. Under ordinary aseptic technic the chest was entered through the fifth intercostal space and the heart exposed. The lungs were retracted and the pericardial sac was opened. A stay suture was passed through the apex of the heart for traction. A wound was then made in the right or left ventricle with a scalpel (Fig. 1) and often enlarged with scissors (Fig. 2) to permit a rather

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† This work was aided in part by a grant from the Upjohn Co. to the University of Chicago.

profuse spurt of blood with each systole (Fig 3) In some instances the wound was made large enough to admit the tip of the finger A sheet of dry, compressed gelatin sponge,\* which had been cut to approximately one and one-half inches in diameter, was applied over the spurting wound and held in place by the operator's fingers with moderate pressure synchronized with the contractions of the heart while traction was made on the suture passed through the apex (Fig 4) Pressure was maintained over the patch for three to five minutes for wounds of the right ventricle and five to 13 minutes for wounds of the left ventricle After this period of time the "patch" was usually sufficiently



FIG 1—Showing scalpel wound of left ventricle

adherent to control the hemorrhage completely After 20 to 30 minutes the "patch" was usually firmly adherent to the heart and sometimes difficult to remove because of its "fibrin fixation" to the wound (Fig 7) The pericardium was sutured and the wound in the chest closed with silk after re-expanding the lungs with the intratracheal positive pressure and withdrawing any residual air in the pleural cavity by a catheter which was withdrawn as the last suture was placed in the wound

During the period of pressure on the patch, the sponge was permitted to become saturated with blood (Fig 5) It was a rather important point in the

\* The gelatin sponge used in these experiments had been heat sterilized and packaged in large sealed glass jars by the manufacturer The sponge was provided in the form of sheets measuring  $3\frac{1}{4}$  inches by  $4\frac{3}{4}$  inches by  $\frac{1}{2}$  inch When compressed the sponge measured about  $\frac{1}{8}$  inch in thickness The smaller pieces of sponge which had been commercially available were found to be entirely inadequate in controlling massive hemorrhage such as was produced in these experiments



FIG 2—Showing wound of ventricle being enlarged with scissors



FIG 3—Showing hemorrhage from wound of left ventricle

technic to maintain even pressure on the patch so that when the blood clotted in the sponge, the "patch" would become adherent about the wound as a result of the liberation of fibrin during the clotting process (Fig 6) If the blood



FIG 4—Showing "patch" of dry compressed gelatin sponge applied over spurting wound of left ventricle



FIG 5—Showing "patch" of gelatin sponge being held in place over wound of left ventricle after it has become saturated with blood

clotted in the sponge before even pressure was obtained, the "patch" would not adhere sufficiently to control the hemorrhage completely. In several instances it was necessary to reinforce the original "patch" or apply a fresh one on the wound. This latter was found to be more satisfactory.

Another point in technic was to avoid having the "patch" become adherent to the gloved fingers while pressure was being maintained. The dry compressed sponge would stick to the gloved fingers very easily. Moistening the gloves with saline solution just before applying the "patch" would usually suffice to prevent this. In subsequent experiments on the use of the "patch" for wounds of the auricles an improvement in the technic of applying the "patch" was worked out.<sup>6</sup> This consisted of using a piece of perforated Cilkloid over the "patch" to prevent the sponge from sticking to the gloves. The Cilkloid would become adherent to the "patch" if there was any remaining sponge which was not soaked by blood. By applying a few drops of saline over the Cilkloid, it would penetrate the perforations and moisten and soften the sponge



FIG 6—Showing "patch" of gelatin sponge which has become adherent to heart due to the clotting of blood in the sponge and completely controlling hemorrhage from wound in heart (left ventricle)

so that the Cilkloid could be easily removed without danger of dislodging the gelatin sponge patch. Needless to say the Cilkloid should always be removed as there is no evidence that it would become absorbed, and furthermore it is possible that its behavior in the tissues would resemble that of cellophane.

#### RESULTS

In a series of 15 experiments, the wound was made in the right ventricle in 4 and in the left ventricle in 11. The hemorrhage was completely controlled by the application of a gelatin sponge "patch" and the animal survived the immediate postoperative period. In six other experiments, the animal died from ventricular fibrillation when the pericardial sac was opened or when the wound was made in the heart. Novocaine solution and electrical stimulation were used in an attempt to prevent or arrest ventricular fibrillation. These



measures were, for the most part, relatively ineffective. The most satisfactory means of preventing fibrillation appeared to be careful handling of the heart and especially avoiding torsion. Most of the instances of ventricular fibrillation occurred in the earlier experiments. In addition to these procedures, three acute experiments were performed without asepsis to work out points in the technic of applying the sponge. In these experiments the "patch" was applied, removed, and fresh "patches" reapplied as many as six times, with complete control of hemorrhage in each instance. These animals were sacrificed at the end of the experiment.



FIG 7—Showing gelatin sponge firmly adherent to heart 30 minutes after application of "patch." It is difficult to remove patch after this length of time due to the "fibrin fixation" of the sponge to the heart wound.

In the series of 15 animals which survived the wound of the heart to which the gelatin sponge "patch" was applied, five died between two and 12 days from distemper, pneumonia, or empyema. One died after three days from pneumonia but also had an intracardiac thrombosis due to the migration of the sponge "patch" into the cardiac chamber. In this particular experiment, the sponge was applied over a very large wound and it was necessary to place a second "patch" over this. It was the under "patch" which worked itself into the wound and contributed to the intra-cardiac thrombosis. Eight of the animals were sacrificed on the 4th, 18th, 24th, 40th, 68th, 73d, 92nd, and 104th day, and one was sacrificed after 6 months.

The heart specimens were photographed (Fig 8), the cardiac chambers were opened, and sections were taken through the wound in the myocardium for microscopic studies. In two of the animals, there was a greyish appearance



FIG 8—Showing gross specimen of heart at autopsy at varying periods of time after application of gelatin sponge "patch" for control of hemorrhage from wound of heart

A After four days



FIG 8B—After nine days

to the pericardial sac suggestive of an early pericarditis although no exudate was present. This was usually associated with an extensive distemper, pneumonia, or empyema.



FIG 8C—After 18 days



FIG 8D—After 40 days. The sponge has undergone partial absorption.

In none of these experiments was there any evidence of accumulation of blood in the pericardial sac to suggest that secondary hemorrhage had occurred from dislodgement of the "patch." The closure of the pericardium appeared to be adequate additional support to the sponge to prevent subsequent blowing off

of the "patch" There was no evidence of aneurysm formation in the ventricular wall where the wound was produced in any of the specimens examined

At autopsy the gelatin sponge "patch" was very firmly adherent to the heart, and usually only lightly adherent to the overlying pericardium There was very little evidence of adhesions within the pericardial cavity except where the sponge was present As the sponge underwent absorption, the adhesions present tended to regress

From the gross standpoint, the sponge appeared to undergo absorption in about two months In the microscopic studies, an early stage of sealing off of



FIG 8E—After 68 days The gelatin sponge has undergone absorption and there is a residual fibrous tissue scar overlying wound which was adherent to pericardium

the wound by the gelatin sponge "patch" and filling of the wound by a blood clot was seen Relatively rapid fibroplasia was found to develop, uniting the wound and the intact muscle under the cover of the gelatin sponge After several weeks the wound was healed by a well differentiated fibrous tissue scar (Fig 9)

In two instances there was calcification in the healed scar of the myocardium The gelatin sponge apparently produced relatively little inflammatory reaction and it was unusual to see much of a polymorphonuclear invasion in the

early stages except in those animals where there was a complicating infection. There was replacement of the sponge by fibrous tissue due to the invasion of the sponge by fibroblasts during the period of healing of the wound.

The rate of absorption of the sponge as determined by microscopic studies was found to be somewhat slower than was observed in previous work. In one instance there was evidence of a few remnants of the sponge in a thin fibrous scar as late as three months, although the sponge was usually completely absorbed in about two months.



FIG 9A —Showing photomicrograph of heart after nine days. The gelatin sponge "patch" covers wound in which extensive fibroplasia has filled in the defect in the myocardium. In addition there are areas of calcification in the healing wound.

#### COMMENT

The control of hemorrhage from a wound of the left ventricle by the use of dry, compressed gelatin sponge without the addition of thrombin or supplementary suturing represents a critical experimental test of the effectiveness of this hemostatic agent. Furthermore, this study has given additional information on the mode of action of the gelatin sponge.

It would appear that the sheet of dry, compressed gelatin sponge acts more or less like a tampon which stops the stream of blood coming out of the wound. When the sponge is soaked in saline it is so soft and so easily permeated by blood that it does not lend itself to controlling a forceful stream of blood such



FIG 9B—Showing photomicrograph of healed wound in left ventricle with remnants of gelatin sponge overlying the fibrous scar which can be traced through the wall of the ventricle after 40 days

as one encounters from the left ventricle. As the dry sponge is held over the wound enough blood escapes through the intercommunicating interstices to saturate the sponge. When the blood clots in the sponge one has obtained essentially a reinforced clot with the sponge architecture offering a framework for the clot. As the blood clots in the sponge, fibrin is liberated and produces

an increasingly strong adherence of this reinforced clot or "sponge clot" to the wound provided that even pressure is applied over the sponge during the clotting process. It is necessary to maintain this pressure until the adherence of the "sponge clot" to the wound is sufficiently strong that it will withstand the force of the blood from the cardiac chamber. This was found to require as long as 13 minutes in some of the experiments on the left ventricle although only three minutes was required in some wounds of the right ventricle.

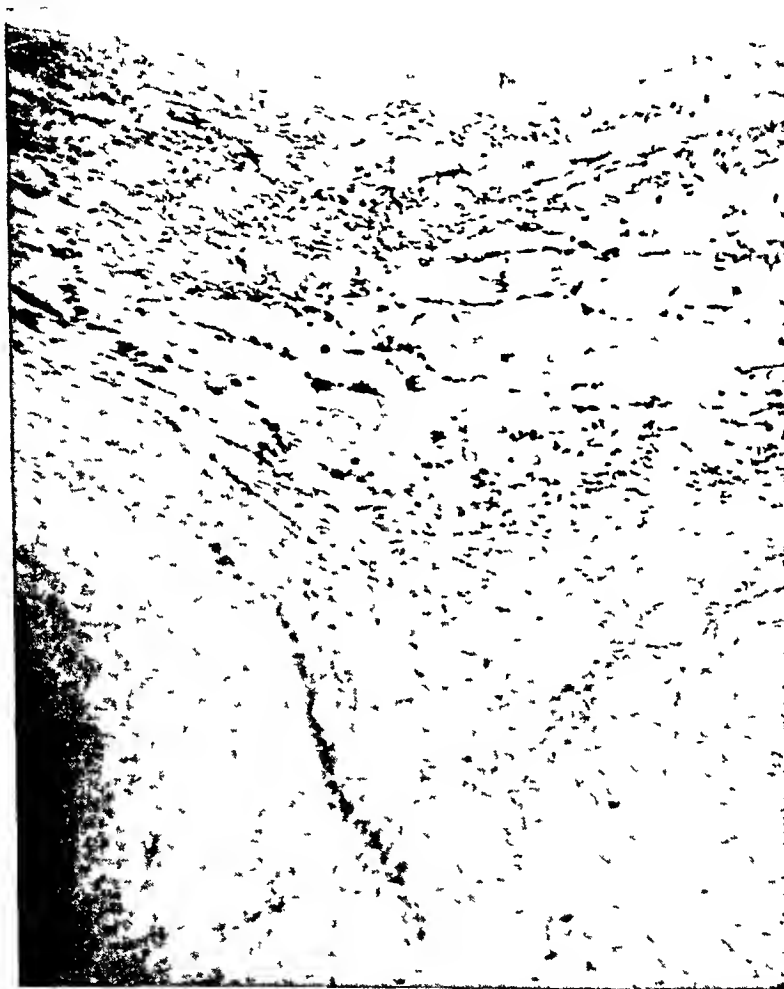


FIG 9C—Showing photomicrograph of heart 68 days after application of gelatin sponge "patch" to wound. There is a residual fibrous plaque replacing the gelatin sponge and covering the fibrous scar in the myocardium.

In view of the fact that thrombin was not used with the gelatin sponge in these experiments it would suggest that the clotting was brought about by a combination of factors. The stopping of the stream of blood from the heart wound by the tampon effect of the dry sponge is one important factor. In several instances where relatively small wounds were made, especially in the right ventricle it was possible to remove the gelatin sponge "patch" after about 10

## GELATIN SPONGE IN HEART WOUNDS

minutes without having a resumption of the hemorrhage from the wound due to the formation of a clot which sealed the wound edges together. On the other hand the removal of a "patch" would usually result in the resumption of hemorrhage in most instances. One of the principle sources of thromboplastin is heart muscle and it is probable that in wounds of the heart there may be an appreciable amount of clot stimulating material liberated which enters the sponge along with the blood and thus hastens the formation of a clot in the sponge as well as in the wound. Furthermore, the enormous surface area of

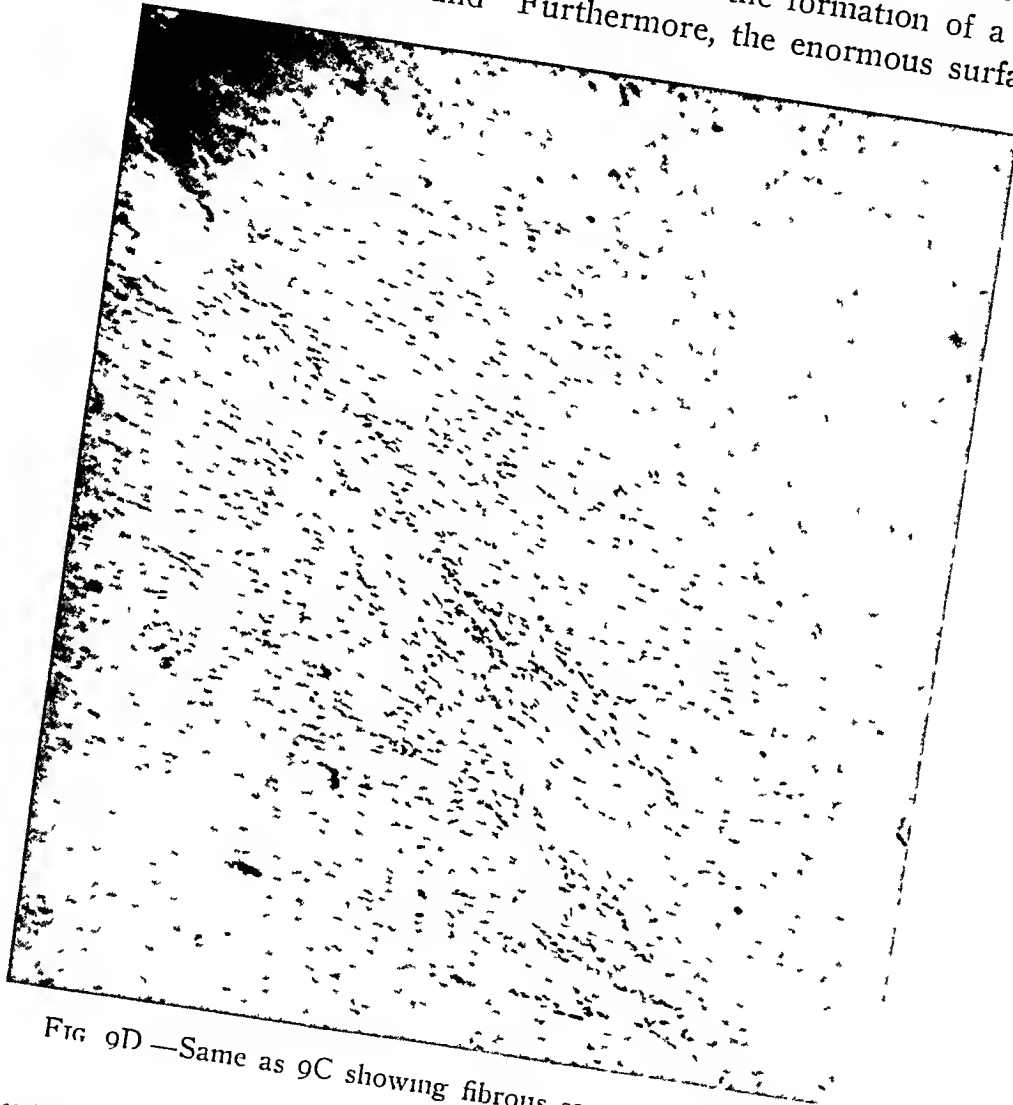


FIG 9D—Same as 9C showing fibrous scar in myocardium

the many interstices of the sponge would undoubtedly cause damage to the platelets, thus liberating thromboplastin from this source. The thromboplastin along with the calcium and prothrombin of the blood probably produced enough thrombin to initiate the clotting mechanism by its action on the fibrinogen.

Aside from the hemostatic effect of the sponge, it should also be pointed out that the sponge "patch" provided protective cover to the wound and gave it support during the process of wound repair. This was also observed in previous studies. After completing its primary role as a hemostatic agent and its secondary role of protection and support of the wound during the healing



process, the gelatin sponge underwent absorption with nominal tissue reaction

It is very important to emphasize that the successful use of the gelatin sponge revolves about attention to the details in the technic of applying the sponge. This may come only from actual experience in handling this material

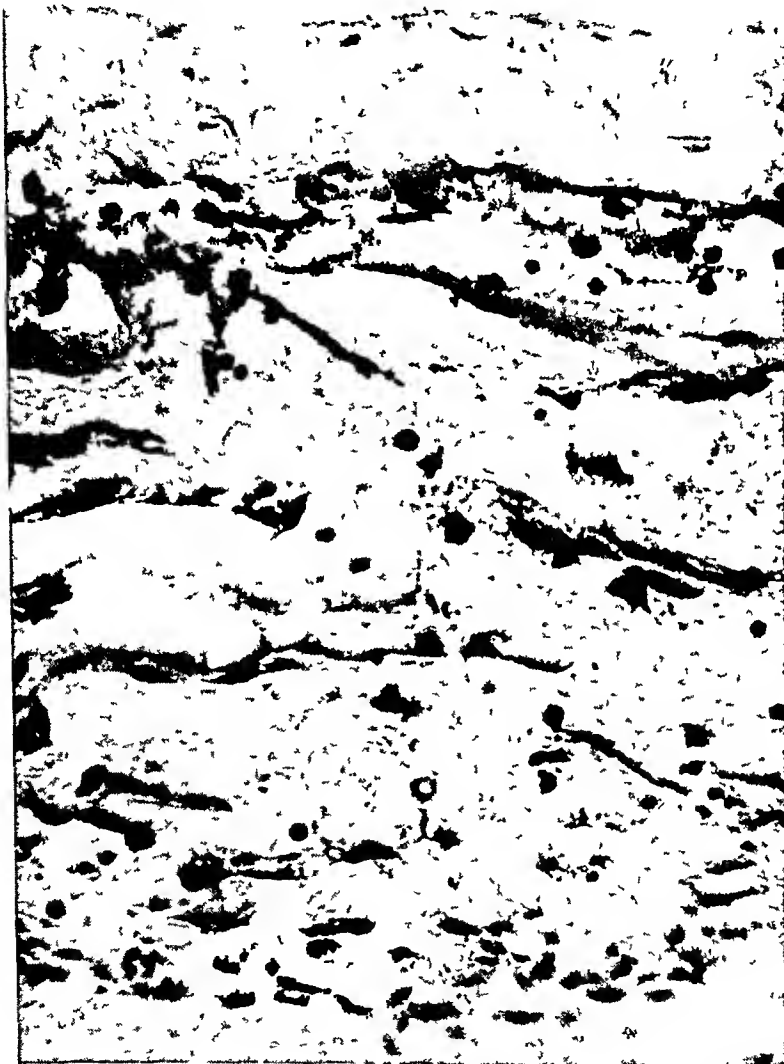


FIG 9E—Same as 9C showing higher magnification of fibrous plaque overlying wound in which a few spicules of gelatin sponge can still be detected. These remnants are undergoing the terminal phase of absorption by the action of the adjacent macrophages

In addition, an understanding of the mode of action of the sponge in obtaining hemostasis aids in working out the technique which may be applicable to any particular problem of hemostasis.<sup>7</sup>

In view of the results obtained in this experimental study, it would suggest that the gelatin sponge may have a place in the surgical treatment of penetrating wounds of the heart

Since the first successful suture of a wound of the heart by Rehn in 1896<sup>8</sup>

there have been many advances in surgery of the heart. The principal contributions to the treatment of wounds of the heart have been made by Elkin,<sup>9</sup> Bigger,<sup>10</sup> Beck,<sup>11</sup> Singleton,<sup>12</sup> Griswold and Maguire,<sup>13</sup> and Linder and Hodo.<sup>14</sup> With improvement in operative technic and asepsis, and with attention to administration of intravenous fluids preoperatively as advocated by Cooper and co-workers<sup>15</sup> it has been possible to obtain increasingly satisfactory results from suture of wounds of the heart. This is demonstrated by the most recent series of cases reported by Elkin where a mortality rate of 22 per cent was obtained.

Blalock and Ravitch<sup>16</sup> have drawn attention to the desirability of conservative management of selected cases of wounds of the heart by resorting to aspiration of the pericardial sac to relieve the cardiac tamponade. In the presence of continued bleeding into the pleural cavity or through the chest wound or if evidence of cardiac tamponade recurs after aspirations they feel that immediate cardiorrhaphy should of course be performed.

Although we have presented a non-suture experimental method of dealing with wounds of the heart, in the clinical application of this experimental study we are not prepared to suggest that the gelatin sponge should be used to replace suture.

One of the main problems in the handling of stab or bullet wounds of the heart in patients is the massive hemorrhage which one may encounter as one opens the pericardial sac. The gelatin sponge may provide a means of obtaining immediate control of hemorrhage from a wound of the heart and at least momentarily preventing further loss of blood. It is thoroughly possible that with the hemorrhage controlled in this fashion, one could then very gently peel back the sponge and insert sutures in a relatively dry field. Or the sutures may be placed in the wound and tied over the patch of sponge covering the wound.

Another point which suggests itself is that the gelatin sponge may provide a secondary line of defense after sutures have been placed in the wound and thus serve as an additional safeguard against leakage from the suture line. This may make it possible to place fewer sutures and to tie them with less tension, thus lessening the danger of ischemia of the cardiac muscle or of initiating a stimulus which may precipitate ventricular fibrillation.

Finally, in relatively small wounds, or in wounds which are adjacent to coronary vessels, it is possible that the gelatin sponge "patch" alone may suffice. The clinical evaluations of this experimental method must be made by those who have had the widest experience in the treatment of penetrating wounds of the heart. It has come to our attention that the gelatin sponge has been used in two instances as a supplement to suture of a wound of the heart.<sup>17</sup> In one of these cases it was especially useful in controlling bleeding where the stay suture had been placed for traction.

Furthermore, it is hoped that some modification of this gelatin sponge patch method may be helpful in controlling hemorrhage in other types of cardiac surgery, such as for valvular stenosis or foreign bodies.

## SUMMARY

In a series of 15 experiments on dogs, it has been possible to control hemorrhage from relatively large wounds of the right or left ventricle with a "patch" of gelatin sponge without any supplementary suture or the use of thrombin in the sponge

The fundamental principles involved in the control of hemorrhage by the gelatin sponge "patch" is essentially as follows. When the dry compressed gelatin sponge is applied over the spurting wound it acts first of all as a tampon to slow down and stop the massive flow of blood through the wound. As the sponge becomes saturated with blood, clotting occurs in the sponge, thus forming a "reinforced clot." During the clotting process fibrin is liberated, which permits this reinforced clot or "sponge-clot" to adhere to the heart. In applying the "patch," it is therefore necessary to allow the sponge to become soaked with blood and then to maintain firm even pressure over the sponge until sufficient fibrin is liberated to produce the adhesive effect which is so essential to the control of the bleeding. Healing progresses under the protective cover of the sponge while the sponge gives support to the wound during this healing phase. The sponge ultimately undergoes absorption.

## CONCLUSION

In view of these experimental observations, it would appear that the gelatin sponge may have a place in the treatment of wounds of the heart to control the immediate hemorrhage, as a supplement to suture, or possibly as an alternate to suture under special circumstances such as proximity of the wound to a coronary vessel.

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## ANNOUNCEMENT

### UROLOGY AWARD

THE AMERICAN UROLOGICAL ASSOCIATION offers an annual award of \$1,000 00 (first prize of \$500 00, second prize \$300 00 and third prize \$200 00) for essays on the result of some clinical or laboratory research in Urology. Competition shall be limited to urologists who have been in such specific practice for not more than five years and to residents in urology in recognized hospitals.

The first prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Hotel Statler, Boston, Massachusetts, May 17-20, 1948.

For full particulars write the Secretary, Dr Thomas D Moore, 899 Madison Avenue, Memphis Tennessee. Essays must be in his hands before March 1, 1948.

# FAMILIAL HEMOLYTIC ANEMIA AND ITS SURGICAL ASPECT WITH SPECIAL REFERENCE TO A CASE COMPLICATED BY THE RH FACTOR\*

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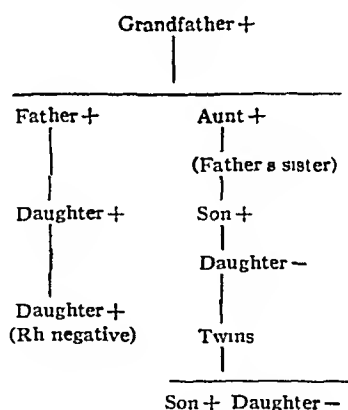
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THE OCCURRENCE OF A CASE OF FAMILIAL HEMOLYTIC ANEMIA in the Pfeiffer Surgical Clinic of the Abington Memorial Hospital, which was complicated by the Rh factor and presented certain other interesting factors, prompted the authors to report the case and review the literature

Familial hemolytic anemia, known for years as congenital hemolytic jaundice, may appear in the infantile form striking at birth, or be latent appearing anywhere from birth to the fifth decade, but less frequently after the third It is believed to be a Mendelian dominant, but there is no regularity in its transmission nor severity

TABLE I  
THE PENHALLOW FAMILY



\* + victims of disease

It is interesting to note that the Rh factor is dominant and follows the Mendelian law of inheritance<sup>9</sup> However, checking the Rh factor of this family showed that only one daughter was negative

The acute exacerbations of this disease, we believe, are the result of some activation, possibly some antigen agglutinin or other allergic reaction Once the activity begins it is apt to continue until the site of the increased hemolytic activity is removed

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### SYMPTOMATOLOGY

The symptoms of the disease are varied, but at no time appear to be very severe except during a crisis, and the patients are therefore rarely incapacitated, although they may be running a markedly elevated temperature, and be quite icteric, so much so that Chauffard remarked that the patients are "more jaundiced than sick." The jaundice varies in degree, but usually mild—being yellow or frequently sallow, rather than brown or green. Pruritus and bradycardia, so frequently a concomitant finding in jaundice, are not present.

The patients as a rule are subject to moderate weakness, malaise, and headaches. During a hemolytic crisis, which is an exacerbation of increased hemolytic activity, all the symptoms are increased, particularly the fever which may reach  $105^{\circ}$  or  $106^{\circ}$  without showing any marked effect on the patient's general well being, although in our experience gastro-intestinal symptoms, *i e*, nausea, abdominal pain, and diarrhea, are usually present.

The crises of hemolytic jaundice may be classified by various prominent features. Gripwall<sup>6</sup> classes them as (1) thermic, (2) abdominal, (3) essential blood crises. Thermic crises, apart from other aspects of the disease, are not clear. Abdominal crises apparently are associated with changes in liver function and structure, and not necessarily with increased blood destruction. The essential blood crises are what we commonly associate with acute crises of congenital hemolytic jaundice, and are of the hemoclastic type producing severe, even fatal anemia. The nature and relationships of the above three types cannot be definitely established as yet.

The spleen which is enlarged in nearly every active case and usually extends to the level of the umbilicus or below, may enlarge considerably during crises accompanied by more or less severe upper left quadrant pain due both to the stretching of the capsule and to occasional infarcts.

The liver may also be enlarged and during a crisis may likewise be quite tender. Liver crises according to Lewis<sup>1</sup> "may be precipitated by the passage of thickened bile through the ducts." Gastro-intestinal symptoms, as a whole, are common, but being referable particularly to the gallbladder. Hepatitis, cholecystitis, and cholelithiasis are common and give symptoms characteristic of these disorders.

Unexplained obdurate ulcers of the foot and ankle have been frequently observed. Osseous changes, such as thickened and enlarged parietal and frontal bones and mottling of the marrow spaces, also occur not infrequently (Turmschadel).

### LABORATORY STUDIES

Blood studies are quite pathognomonic of the disease. The anemia which is microspherocytic in form may vary from three or four million to one million during a crisis. The color index and mean corpuscular hemoglobin are usually high. The mean corpuscular volume may be increased despite small mean corpuscular diameter. Anisocytosis is quite frequent and microspherocytosis is the conspicuous feature. Poikilocytosis may also be present. Reticulated red cells vary with the need of increased blood production and may vary from 2

to 60 per cent. Nucleated red cells are usually constant, showing evidence of cell regeneration. Usually the increased fragility of the red cells to the hemolytic action of hypotonic salt solution is characteristic, but it may be normal or even lessened if the reticulocyte count is elevated. The white cell response is not characteristic, but most frequently there is a leukocytosis with a polymorphonuclear increase. The platelets are usually normal.

The plasma volume is usually decreased, therefore the quite frequent dehydrated appearance of these patients.

The blood chemistry is not usually markedly altered. The serum bilirubin is moderately elevated, and there is an immediate indirect Van den Berg reaction. In mild cases it averages 1-4 mg/100 cc, and in more severe cases 10-20 mg/100 cc. Hemoglobinemia has been detected in severe hemolysis. Blood cholesterol may or may not be elevated, though fat metabolism is usually normal as is protein metabolism. Iron elimination, however, is considerably increased.

Urine is usually dark, but contains no bile (acholuric jaundice) except during liver crises. Urobilin and urobilinogen are constantly present.

Pathology of the reticulo-endothelial system is quite characteristic, particularly that of the spleen which, according to Thompson, is constant and diagnostic of familial or spherocytic jaundice. It is usually large weighing between one and two kilograms. The weight in our Rh negative case was 2.9 kilograms. This, we believe, to be the heaviest spleen reported for this disease. The capsule is usually somewhat thickened, but adhesions are rare except over infarcted areas. The cut surface is dark red and convex, bulging above the capsule. The framework of the spleen is not maintained, and malpighian bodies are not seen grossly, but on microscopic examination are small and normal in number in proportion to the splenic size. The pulp is characteristically engorged by red cells so that the pulp cells are scant, and there is no noticeable increase in connective tissue framework.

The venous sinuses are markedly dilated and lined by two or three layers of large endothelial cells. Although there is no general increase in iron pigment, iron incrustation within the trabeculae is not infrequent and siderofibrotic nodules are occasionally seen. There is no definite evidence of phagocytosis.

Other tissues of reticulo-endothelial composition show evidence of pigment deposition. The bone marrow is red and hyperplastic with numerous normoblasts and myelocytes. Ectopic myeloid tissue is sometimes encountered along the vertebral bodies. The liver is occasionally cirrhotic probably due to liver damage brought about through previous episodes of marked anemia and anoxemia.

#### PATHOGENESIS

The pathogenesis of this disease is still a much discussed topic, and therefore the various theories will only be alluded to briefly. The fundamental fault is increased blood destruction either through exaggerated normal processes of blood destruction or through wholly abnormal processes. The normal process in the spleen is fundamentally fragmentation supplemented by the action of

certain cells in the spleen and other parts of the body in further breaking down corpuscular fragments<sup>1</sup> However, erythrophagocytosis and hemolysis have never been demonstrated in the normal process Therefore, in abnormal blood destruction several possibilities appear The cells may be more fragile than normal, the blood serum may contain destructive agents, or erythrophagocytosis may be present<sup>1</sup>

Thompson believes that increased fragility is the only deviation from normal necessary to produce the disease, and that spherocytes are formed by abnormal erythropoiesis Dameshek and Schwartz, however, show evidence that the microspherocytosis is just one of the steps in the process of hemolysis They also bring forth the argument that microblasts and reticulated microcytes are infrequently found in the peripheral blood and bone marrow in this disease Overproduction of hemolysins or underproduction of anti-hemolysins, both of which are found in balance in normal serum, may result in free hemolysin In other abnormal blood states, auto-agglutinins, auto-hemolysins, iso-hemolysins have been found, and it is conceivable these may be the cause of the hemolysis in this disease

Dameshek and Miller believe that hemolysis is an active process due to red cell injury by a variety of agents, such as, pure hemolysins, complex hemolysins, or agglutinins<sup>7</sup> Spherocytosis, as seen in this disease, indicated incomplete hemolysis by means of the activity of some hemolytic agent, but which may not be readily identified This spherocyte then, they state, may become completely hemolyzed by erythrosthesis which therefore is only of secondary importance to the primary action of the hemolysin

The part that the spleen plays in this disease has always been of some debate Is it primarily the site of the abnormal blood destruction, or is it only an accessory to an otherwise stimulated hyperfunction elsewhere? Dameshek and Miller feel that the spleen is more than simply an organ of stasis, but may have an active hemolytic function as well, particularly in acquired hemolytic anemia We must not lose sight of the fact that it does take an active part in the normal process of blood destruction, that in familial hemolytic jaundice it undergoes marked hyperplasia as well as hypertrophy, and that improvement follows splenectomy in the typical familial case

#### THERAPY

The treatment of the disease is not an emergency for, as it has been noted, the symptoms of the disease are not distressing except in crises The duration of life is not shortened nor are the patients incapacitated, except during crises, or because of a large abdominal tumor, although the latter usually in itself is not troublesome except from the cosmetic standpoint The studies of this family, as well as other family groups made in the Abington Memorial Hospital,<sup>8</sup> suggest that perhaps we should be bolder in advising surgical treatment with a view of preventing crises

It has long been thought that transfusions were of great benefit in hemolytic anemias, particularly in sickle cell and Lederer's acute secondary hemo-



lytic anemia They have been used for a long time as one of the most important parts of the therapy of congenital hemolytic icterus, but many clinicians advise against their use in this disease as they may be the trigger mechanism in setting off an acute crisis, and may even prove fatal if given during a crisis Farr has reported such a case in which the clinical condition was aggravated by transfusion—showing moderate liver degeneration with recovery following splenectomy This suggests that an acute liver failure is one of the pathogenic mechanisms of the clinical crises observed in the hemolytic anemia Lowe<sup>1</sup> has demonstrated quite accurately that during a crisis, a form of acute hepatitis frequently occurs with diminished liver function, as demonstrated by liver function tests and pigment conversion and excretion In one such episode, the patient was transfused and appeared to improve, but in another attack no transfusion was given and improvement was just as dramatic and rapid

TABLE II

<p>B P Rh negative patient 2/4/46 Coag time 5½ min Bleeding time 2½ min Platelets 328 000 Fragility hemolysis begins 0 46% completed 0 32% NaCl Hemoglobin 15 5 Gm 102% Red count 4 970 000 White count 9 000 Polys 60 Lymphs 37 Monocytes, 3 Prothrombin 65% Icterus index 6 Van den Bergh direct delayed indirect 0 6</p>	<p>White count 7,400 000 Polys 66 Lymphs 30 Monocytes 4 Prothrombin, 80% Icterus index 5 Van den Bergh direct delayed indirect 0 5</p>
<p>D H sister 2/4/46 Coag time 6 min Bleeding time 1 min Platelets 409 000 Fragility hemolysis begins 0 44% completed 0 32% NaCl Hemoglobin 100% Red count 5 100 000</p>	<p>C P father 2/4/46 Coag time 5 min Bleeding time 1½ min Platelets 307 000 Fragility hemolysis begins, 0 44% completed 0 32% NaCl Hemoglobin 14 2 Gm 92% Red count, 4 620 000 White count 8 400 Polys, 63 Lymphs 35 Monocytes 2 Prothrombin 60% Icterus index 6 Van den Bergh direct delayed indirect 0 6</p>

It may then be stated that transfusing during a hemolytic crisis shows a preliminary decrease in blood destruction, but followed by a definite increase, and therefore an increase in clinical symptoms The spleen and liver become large and more tender, and pigment production increases markedly Bone marrow function is likewise suppressed, as evidenced by a drop in red cells, nucleated red cells, hemoglobin and reticulocytes<sup>4</sup> These findings are substantiated by like findings in our series

The only effective treatment is splenectomy which is usually followed by the disappearance of all symptoms It has been stated that the signs of the disease, spherocytosis and increased fragility, persist indefinitely after splenectomy However, the serum bilirubin and urobilin excretion becomes normal and the anemia definitely improves The follow-up blood studies on three of the members of this family, taken a year or more after operation, are shown in Table II

These essentially normal findings, along with blood studies made on nine other patients from one to three years after splenectomy for this disease, lead us to take exception to the above statement that severe spherocytosis and increased fragility persist indefinitely after splenectomy

Operation is usually contraindicated during an acute hemolytic crisis, but may be undertaken in the course of an unusually prolonged or severe exacerbation of hemolytic activity, if the diagnosis is accurate. Our operative mortality for splenectomy in this disease during the past five years in the Pfeiffer Surgical Clinic for 21 cases has been zero

During an acute attack, plasma infusions are the only form of approved therapy, blood being contraindicated in many cases due to the presence of agglutinin—agglutinogen reactions. Operative procedures during these attacks should only be attempted if other complications arise such as uncontrollable hemorrhage or dangerously progressive hemolysis

#### CASE REPORT

B. P., a 21-year-old white female, presented herself for admission to the Abington Memorial Hospital on November 14, 1944 with the chief complaints of abdominal mass, malaise, occasional nausea, and chills and fever

*History of Present Illness* Patient has had an enlarged abdominal tumor, presumably spleen, since birth, at which time she was quite jaundiced. Patient experiences no pain or discomfort from the abdominal tumor except for small food capacity. She has episodes about two months apart of severe jaundice with malaise and vomiting productive of sour bile tinged material. Her skin has always been a trifle icteric

*Systemic Review* Gastro-intestinal—Avoidance of fatty foods, but no actual qualitative dyspepsia. Good appetite but small capacity

Genito-urinary—Menses have always been irregular with quite severe dysmenorrhea. No urinary symptoms

Cardio-respiratory—Dyspnea on exertion. Frequent colds

Neuromuscular—Negative

*Past Medical History* Except for the usual childhood diseases, the past history was negative except for one rather significant fact, *i.e.*, in her early teens she had a sinus drainage at which time she received her first transfusion and suffered a rather severe reaction with chills and fever

*Family History* Father and paternal grandfather have splenomegaly with exacerbations of jaundice accompanied by abdominal pain. Father's sister and two of her four children are similarly affected. Patient's sister has mild splenomegaly. Family on mother's side gives no history of the disease

*Physical Examination* T—100, P—84, R—20 on admission

Examination revealed nothing of note other than that of the skin and abdomen

The skin was of a distinct icteric sallow appearance. The right ankle presented on the external malleolus, a chronic ulcer of four years duration which was about 6 x 6 cm., mildly tender at the periphery, and at times spontaneously productive of pain

The liver edge extended approximately three fingers below the right costal margin. The left abdomen from the costal margin and the lateral border of the erector spinae down to the iliac crest was completely filled with a large firm mass which crossed the mid-line into the right abdominal fossa at the level of the iliac crest, moving freely on respiration, and which was tender only on firm pressure

*Clinical Impressions* The history of long standing jaundice, the splenomegaly and hepatomegaly, the exacerbations of jaundice associated with severe abdominal pain, nausea, and chills and fever, and the apparent high familial incidence of jaundice, and the

splenomegaly on her father's side, led us to make the tentative diagnosis of acute familial hemolytic icterus

*Clinical Progress While in Hospital* Nov 14 —Admitted with red cell count of 2,690,000, hemoglobin of 69 Gm 44 per cent

Blood type A, not typed for the Rh factor

Nov 16 —500 cc of compatible blood Not crossed for Rh factor

Nov 17 —Menstrual period started with moderate dysmenorrhea

Temperature spiked to 103° and was suggestive of transfusion reaction Typed for Rh and found to be Rh negative, a fact that should have been suspected from the history of having had a severe reaction following a transfusion in childhood

Hemoglobin was 38 Gm 24 per cent, and red cell count, 1,670,000

Icterus index 24, Van den Bergh indirect 25, direct delayed

Fragility hemolysis begins 0.80 per cent completed 0.50 per cent

Nov 19 —Patient was assumed to be in an acute hemolytic crisis She complained of some nausea and abdominal pain with chills and fever ranging between 99° and 103°

RBC of 1,510,000, hgb 29 Gm 19 per cent

500 cc of plasma given

Nov 21 —Temperature still spiking Urine urobilinogen qualitatively and quantitatively positive, 1:50 dilution 500 cc plasma given It was decided to give patient test of blood, 100 cc of compatible whole blood Rh negative type O was started intravenously Only 50 cc given because of marked reaction with chills and fever to 103° F Van den Bergh taken before blood was given revealed delayed direct and indirect of 2 mg Test taken three hours after 50 cc whole blood, revealed delayed direct and indirect of 3 mg This 1 mg rise was sufficient to indicate increased hemolysis

Nov 22.—500 cc plasma given Hbg 36 Gm 23 per cent, RBC 1,460,000 Reticulocyte count 3.4 per cent Prothrombin 60 per cent

Nov 31 —Temperature subnormal last four days Now ranging between 98° and 100° F

Dec 1 —Splenectomy

*Operative Report* On December 1, 1944, under general anesthesia, the patient was operated upon by Dr J Walter Levering A left pararectus muscle displacement incision was made, displacing the rectus muscle medially The peritoneal cavity was opened and the spleen, approximately 15 inches in length came into view immediately beneath the peritoneum Its surface was smooth, glistening and of a greyish hue The intestines were then packed out of the way, and the hilus of the spleen identified Because of the size of the spleen it was impossible to turn it medially, although there were no dense adhesions A large rubber intestinal clamp was then placed about what was believed to be the primary spleen pedicle The pedicle was then clamped by means of several Kelly clamps adjacent to the splenic tissue and distal to the rubber intestinal clamp It was then divided between the Kellys Dissection thus far had been comparatively bloodless, however, at this time on attempting to mobilize the spleen more fully and to identify the remaining vessels, an extremely large vein was unavoidably torn The presence of the intestinal clamp, however, prevented retraction, and the bleeding vein was immediately visualized and clamped The spleen was then delivered from the abdominal cavity in toto Further examination of the abdominal cavity at the site of removal revealed two small marble-like accessory spleens, these were removed It is interesting to note three other gland-like structures adjacent to the large vessels were ligated at their pedicles along with the clamped pedicle of the primary spleen Examination of the diaphragm and splenic site revealed a smooth peritoneal surface which was completely free of any bleeding

The gallbladder was then examined and found to be approximately four inches in length, the fundus blue and slightly distended However, the neck and the proximal 2/3 were opaque and yellow A large stone was palpable at the neck of the gallbladder It was felt, however, inadvisable to attempt further surgery at this time The abdominal

cavity was closed in layers without drainage. The sponge and pack count were correct. Clips were used to close the skin. A large compression bandage and scultetus binders were placed on the abdomen to attempt to restore preoperative intra-abdominal tension.

*Pathologic Reports* Specimen consists of a tremendously enlarged spleen measuring 30 x 16 x 9 cm and weighing 2,950 Gm. The surface is smooth and a dull slate grey color. On section considerable blood oozes from the surface which is dark brownish red homogeneous color. Scattered within the substance are numerous pinhead sized glistening opaque white nodules. On a number of transverse sections nothing further is found which differs from the description of the cut surface.

*Microscopic* The splenic pulp is tremendously engorged, and the sinusoids are dilated and filled with red cells and hemosiderin. There is surprisingly little fibrosis. The malpighian follicles are large and have prominent central secondary follicles. There is no evidence of neoplasm or inflammation (Fig 1).

*Report of Gland-Like Accessory Structures* Gross The specimens consist of two smooth-walled bluish red nodules measuring 12 x 9 x 7 mm and 10 x 8 x 8 mm respectively. The former nodule has rather a homogeneous nature and is more suggestive of lymphoid tissue than splenic. The other nodule on section shows a homogeneous dark red substance with a few tiny opaque pinhead sized nodules throughout. This nodule is more suggestive of accessory splenic tissue. One must conclude from the above report that it is difficult to differentiate at operation between an enlarged lymph node and an accessory spleen.

*Microscopic Section* shows one nodule to be lymph node, showing a little hyperplasia and the other a small nodule of accessory splenic tissue.

*Post-Operative Course* Pre-op —RBC 2,620,000, hbg 7.1 Gm 46 per cent

Post-op Immediately RBC 3,320,000, hbg 9.5 Gm 60 per cent

It was felt that this great rise in red cell count and in hemoglobin was due to hemoconcentration.

Dec 2 —Temperature began to rise last night reaching 102° at 9:30 P.M. RBC 3,260,000, hbg 9.5 Gm 61 per cent. 500 cc plasma and intravenous fluids given daily. Patient placed in oxygen tent.

Dec 3 —Temperature reached 103.6° at 4 P.M. and rapidly fell towards normal.

Dec 4 to Dec 7 —Patient has run slightly elevated temperature and has experienced some chest pain. X-ray revealed a left plural effusion, but no lung pathology. RBC averaged about 2,780,000. Hbg averaged about 7.8 Gm 50 per cent.

Dec 11 —Patient was progressing very well, had no transfusions of whole blood but receiving only plasma and infusions. Hoping that we might establish an allergic reaction intradermal injection of Rh+ blood (citrate) was tried, but it gave no sensitivity reaction. Controls run with Rh— blood and with citrate in normal saline.

Dec 23 —Patient discharged from hospital feeling quite well but still running slightly elevated temperature.



FIG 1—Spleen of B. P. RH negative case. Weight 2,950 Gm.

RBC 2,860,000, hbg 66 Gm 43 per cent Reticulocytes 0.2 per cent

As an outpatient, patient appeared for tri-monthly laboratory studies check-up. Seemed to gain strength and weight.

On May 13, 1946, patient returned to the hospital with symptoms suggesting an attack of acute appendicitis. The following day cholecystectomy and appendectomy was done by Doctor Levering. A distended gallbladder with a stone in the cystic duct was removed, as was an acute catarrhal appendix. Thorough search failed to show any accessory spleen. Patient made an uneventful recovery, and was discharged two weeks after admission.

Follow-up studies gave evidence of continued marked improvement following splenectomy. When last seen in February 1947, she was actively working as a waitress. She was very healthy, and even the ulcer on her right ankle that she had had for four years previous to the splenectomy had completely disappeared. Her last blood study, as noted on Chart I, was entirely normal.

#### BRIEF RECORD OF SISTER AND FATHER OPERATED UPON DURING THE SAME PERIOD

*Sister* March 5, 1945, D H, 25-year-old white female, admitted to hospital with the chief complaint of large abdominal tumor of 20-23 years duration and occasional attacks of abdominal pain and jaundice. Patient is now three and one-half months pregnant.

*Past Medical History* Scarlet fever, tonsillectomy, adenoidectomy, and mastoidectomy as a child. Appendectomy performed five years ago, one week after which patient developed jaundice. Patient has had one child followed by puerperal convulsion.

*Family History* This case is the sister of B P, Rh negative.

*Physical Examination* Spleen palpable in left upper quadrant and extending down to level of umbilicus. Uterus palpable two fingers above symphysis pubis. Other findings negative.

*Laboratory Data* Patient presented an anemia of 2,100,000 RBC's and 8 Gm or 52 per cent hemoglobin. Fragility hemolysis begins 0.50 per cent completed 0.36 per cent NaCl. Reticulocyte count was 7.0 per cent on admission, but rapidly was reduced postoperatively to 0.4 per cent 13 days post-operative. Indirect Van den Bergh was 2.8 mg on admission but dropped to less than 0.4 mg before discharge. Blood indices on admission were Volume per cent 28. Mean Corp Vol 101. Mean Corp Hemoglobin 32.6. Mean Corpuscular hemoglobin concentration 31.4. Volume index 1.15, Color index 1.10. Saturation index 0.89. On day of discharge, March 21, 1945, the patient's hemoglobin was 11.8 Gm or 77 per cent, and reticulocytes 0.4 per cent.

Friedman test on admission was positive.

*Operative Report* Operation performed on March 7, 1945, by Doctor Levering, revealed a moderately enlarged spleen and liver, and a markedly diseased gallbladder containing numerous stones. A routine splenectomy and cholecystectomy was performed and patient's convalescence was uneventful. Patient discharged March 21, 1945.

*Pathologic Report* Gallbladder showed infiltration by bile pigment and presented metabolic cholelithiasis.

Spleen showed a picture of congenital hemolytic icterus and weighed 473 Gm.

The patient's follow-up was uneventful and she delivered a normal child at term. The last follow-up blood count is shown on Chart I.

*Father* On February 4, 1945, C P, male, 45, white, the father of the two preceding cases, was operated upon in the Jewish Hospital, Philadelphia.

*Laboratory Findings* Platelets 253,820. RBC fragility began 0.5 per cent completed 0.3 per cent. Blood sugar 93 mg. Blood urea nitrogen 18 mg. Blood count hemoglobin 14.5, RBC 5,180,000, WBC 10,900, neutrophils 67 per cent, lymphs 29 per cent, eds 1 per cent, monos 2 per cent, 1 per cent bas.

*Operative Report* The patient operated upon under fractional spinal anesthesia. The spleen was removed, and weighed 515 Gm. He had an uneventful recovery and his follow-up blood studies, taken about a year later, are shown on Chart II.

CHART I  
SUMMARY OF SIGNIFICANT LABORATORY DATA  
Admission Case B P,—R H,  
—12/1/44—

Hbg Gms and percent	Normals		11/14/44	11/18/44	11/24/44	11/27/44	Pre-op		Post-op	12/4/44	12/21/44	1/12/45	3/19/45
	13 7-17	85-105%	6 9	2 9	4 5	5 1	7 1	9 5	6 1%	8 5	6 6	71%	11 9
			44%	18%	29%	33%	46%	61%	55%	43%			77%
RBC's (thousands)	4,500-5,500		2,690	1,510	1,940	2,240	2,620	3,100	2,780	2,860			
WBC	6,000-8,000		8,200	2,500	7,000	6,400	6,100	13,200	10,200				
Mat neuts	50-70%		63	72	77	79	80	87	91				
Lymphocytes	20-25		30	26	23	20	17	12	7				
Monocytes	4-8		7	2		1	3	2					
Nuclerted reds	0			2	1								
Reticulocytes	Less than 1%		3 4%	3 2%	12 8%	9 8%	12 6%	0 2%	0 5%				
Normoblasts	0												
Prothrombin	70-100%	50%		60%	55%	50%	35%	35%					
Platelets	200,000-400,000				191,000	254,000							
Wassermann	Negative	Neg											
Kahn	Negative	Pos 3 +											
Kline	Negative	Pos 2 +											
Hematocrit	45%								31% vol			40 5%	
Mean cell vol	87	83 cu microns										104	
Mean cell hbg	29 5	26 9 micromicrograms										31 2	

CHART I—Continued  
SUMMARY OF SIGNIFICANT LABORATORY DATA  
Admission

Case B P—R H

12/1/44

Pre op Post op 12/4/44 12/21/44 1/12/45 3/19/45

Mean cell hbg conc	35	11/14/44	11/18/44	11/24/44	11/27/44	12/4/44	12/21/44	1/12/45	3/19/45
		32							
Mean cell diameter	77	62 m							70
Mean cell thickness	195	280 m							
Vol index	100	095							
Color index	100	094							
Saturation index	100	091							
Vol thickness index	100	180							
Diameter to thickness ratio	771.95 or 41	622.8 or 221							
Fragility—Begins Complete	44% 32%	80 50						046 032	
BUN	9-18	15				21			
Plasma NaCl	570-600	610				570			
Plasma CO <sub>2</sub>	50-70	50				45			
Sugar vein	60-90	73							
total protein	6.5-8.0		5.41	6.21	6.45		6.28		
Cholesterol	125-300				184				
Icter index	2-4	24	24	20					
Van den Bergh	Less than 0.4	Direct	Delayed 2.5 mg				Direct neg		
Stool		Delayed and 2 mg	Bile— neg					Ind less than 0.4 mg	

SUMMARY

A review of the symptomatology, the laboratory findings, the pathogenesis, and the therapy for familial hemolytic anemia is discussed. An unusual case of the disease, which was complicated by the Rh factor, is presented in detail. Two other cases in the same family are presented in brief. The follow-up blood studies showing normal figures are presented.

CONCLUSION

The Rh negative case report is of interest because of the complication which arose from blood transfusion.

The giving of plasma rather than whole blood not only in this case, but in other cases is recommended. Plasma infusions will supply the much needed electrolytes, and will elevate the low blood plasma which is present in these cases without the danger of increasing hemolysis.

The tremendous size of the spleen, 2950 Gm., of the Rh negative case is of interest. The recommendation of splenectomy, not only as a beneficial therapy, but also as a curative measure, is recommended.

The follow-up blood studies in our series suggest that splenectomy is not only beneficial in relieving symptoms, but is also curative in these cases of familial hemolytic anemia.

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# ON THE SPECIFIC ROLE OF THE LIVER IN HEMORRHAGIC SHOCK\*†

Report of Progress to Date

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THE CENTRAL DISTURBANCE in traumatic shock, regardless of the nature of the etiologic agent, is a rapid and progressive decline in the velocity of blood flow and a progressive trapping of blood<sup>1, 2</sup> throughout the general capillary bed with a resulting venous anoxemia and a concomitant widespread tissue anoxia. As shock continues, the time arrives when all known therapeutic measures produce no more than a transient, if any, favorable response. When this state of "irreversibility" arrives, the adverse effects of persistent and increasing tissue anoxia become rapidly cumulative with resulting early death.

This statement of the situation is not intended to ignore other factors which, if present, may contribute to the disorganization of the body economy such as gross distortions in fluid and electrolyte balance and damage to specific organs or tissues by specific shock-inducing agents. These are complications that may modify but do not basically affect the primary characteristics of the shock phenomenon.

The tissues which are of vital importance to the co-ordinated activity of bodily processes essential to survival for even a brief interval (minutes to hours) are the central nervous system, the heart, the lungs, and the liver. Total failure of every other organ or tissue except these, in the present state of knowledge, would still permit integrated function consistent with survival over a period of many hours to days. The solution of the problem of such a rapidly lethal phenomenon as the irreversible shock state represents might be approached by considering the disturbances in these vital organs.

## I THE CENTRAL NERVOUS SYSTEM

The vasomotor system has been shown by the earliest workers in the field to be intact until the prelethal phase of shock. (The loss of vasomotion in advanced shock, demonstrated by Chambers and his collaborators,<sup>3</sup> is explained on a humoral basis.) Swingle *et al*<sup>4</sup> revived the theory that nociceptive stimuli from the area of injury induce or intensify shock because spinal anesthesia reduces the incidence of shock from muscle trauma to a lower extremity.

\* Part of the work described in this paper was done under a contract, recommended by the Committee on Medical Research of the Office of Naval Research of the United States Navy and Harvard University.

† Read by title before the Meeting of the American Surgical Association, March 25-27, 1947, Hot Springs, Virginia.

Wang<sup>5</sup> has recently shown a slightly greater tolerance to trauma by denervation of the traumatized extremity. The protective effect of spinal anesthesia, according to Phemister and his co-workers<sup>6</sup> is due to the decreased bleeding consequent to the reduction in blood pressure, while no protection is provided by section of the cord, the nerve roots or all the peripheral nerves to the extremity. Prolonged hypotension induced by stimulation of the cardioaortic nerves produces eventual exhaustion of the vasomotor center, but rapid recovery follows removal of the stimulation at any time before collapse of the vasomotor center. Stimulation of somatic nerves does not produce neurogenic shock. Phemister<sup>7</sup> summarized his work by stating that the neurogenic factor is of little or no importance except that hemorrhagic shock may be intensified by direct nerve stimulation sufficient to produce depression of the vasomotor center.

In hemorrhagic shock the key metabolites involved in biological energy transformations show very little disturbance in brain tissue in contrast to severe depletion of such substances in liver and kidney.<sup>8</sup> Consistent with these findings is the absence of significant signs of brain damage in dogs whose livers have been perfused throughout a prolonged period of hemorrhagic shock and in dogs which have recovered from "irreversible" shock as a result of perfusion of the liver (See below).

There is little or no direct evidence from the foregoing data to incriminate the nervous system in the development of the irreversible phase of shock.

## 2. THE HEART

Cardiac output is much reduced and continues to decline as shock reaches its terminal phase. There is a critical level of cardiac output which, if lowered even slightly by a small withdrawal of blood, results in sudden death. Since temporary improvement in cardiac output always occurs in response to repeated transfusions until just before death, the progressive decline in cardiac output would seem not to be due primarily to functional collapse of the heart. The myocardial weakness demonstrated by Werle, Cosby and Wiggers,<sup>9</sup> and by Kohlsteadt and Page,<sup>10</sup> and by Wiggers<sup>11</sup> is an expected result of prolonged anoxia, which affects the function of all tissues adversely. No bacterial or other toxin directly affecting cardiac function has been demonstrated to operate in hemorrhagic shock. Since a primary disorder in the central circulation has not been shown to exist,<sup>12, 13</sup> the cause of the progressive decompensation in the peripheral circulation must be sought elsewhere.

## 3. THE LUNGS

The lungs may be excluded from consideration because they continue to function adequately (as indicated by full oxygen saturation of the arterial blood until death), except when pulmonary edema results from overtreatment with fluids. Respiratory disturbances are generally due to reflex, metabolic and humoral factors.

## 4 THE LIVER

The extensive biochemical disturbances in shock<sup>14, 15</sup> may result from damage to cellular function in general or from a functional disorder in one or more organs of controlling importance in preserving metabolic equilibrium. There is reason to believe that a biochemical lesion in the liver is responsible for the rapid deterioration of the shock state.\*

Thus the greater resistance to traumatic shock in rats fed a balanced diet as compared to rats on a low protein diet<sup>17</sup> may be correlated with the better respiration of liver slices from prefed rats in hemorrhagic shock than the respiration of liver slices from fasted rats in hemorrhagic shock.<sup>18</sup> LePage demonstrated in traumatic shock marked depletion of high energy phosphate substances in the hepatic and renal cells in contrast to slight depletion of these substances in other tissues.<sup>8, 19</sup>

If damage to the liver can be shown to be extensive enough, the rapid downhill course of the shock state might be explained on this basis alone. The liver receives some three-fourths of its blood supply from the portal vein. This blood, though venous, has an oxygen saturation value of some 15 volumes per cent. In shock this value is 5 per cent or less. Moreover, the volume flow through the portal vein and hepatic artery is greatly diminished. It is clear that great injury to liver function will result if this situation persists for very long.

There is an abundance of data to show that the liver suffers severe injury in traumatic shock. The secretion of bile slows up or stops and along with it bromsulphthalein clearance and other excretory liver functions must do the same.<sup>20</sup> The production of fibrinogen<sup>21</sup> and hypertensinogen<sup>16</sup> is reduced. Deamination in the liver is said to be deficient,<sup>22</sup> although the evidence is not unequivocal.<sup>23</sup> An ordinarily well tolerated withdrawal of plasma, if repeated in the same animal after the liver has been slightly injured, will result in rapidly fatal shock, while severe cell injury to other organs (kidney, pancreas, intestine) does not modify the response.<sup>24</sup> Finally, the friable, congested and discolored state of the liver at death from shock suggests not only the possible total absence of liver function but also the presence of toxic decomposition products.

These data indicate that liver injury may be specifically related to the development of that degree of functional deterioration which nullifies the effectiveness of any known therapeutic methods. Experiments to be described below were devised to test the validity of this hypothesis.

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\* Damage to other organs such as the kidney or adrenal is not of such central importance because, in respect of metabolic effects, the loss of function in these organs is lethal only after several days.

The pressor response of the kidney to ischemia is lost early in shock. This does not implicate the kidney in the genesis of irreversibility because (1) bilateral nephrectomy does not alter the course of the shock state if it is induced before the damage from retention products occurs, (2) even if renin secretion could continue during shock, it would exert no benefit because of the early disappearance of hypertensinogen from the blood.<sup>16</sup>

SUMMARY OF DATA ALREADY REPORTED

If the liver of a dog in hemorrhagic shock is continuously perfused from the onset of the shock state by cross-circulation with a healthy donor animal, the development of irreversibility to transfusion is prevented and recovery from shock occurs<sup>25</sup> The donor dog is apparently unharmed

The cross-circulation set-up consists in a flow of arterial blood from a major artery of the donor into the splenic vein of the recipient (dog in shock) at a rate sufficient to approximate the normal total blood flow through the recipient's liver The same volume of blood returns via both femoral arteries of the recipient to the systemic veins of the donor

If this set-up is arranged so that the blood flow from the donor enters the recipient's systemic veins instead of the splenic vein, the course of the shock state is precisely the same as if no perfusion had been performed i.e., irreversibility to transfusion is not prevented, all the manifestations of rapid and progressive decline appear and death follows, after the usual interval In this case, too, the donor animal fully recovers and is virtually unharmed at the end of the experiment It appears then that perfusion of the liver with arterial blood from a donor protects the liver against damage, while the remainder of the organism is subject to all factors of extrahepatic origin that might be contributing to the development of irreversibility to transfusion To determine the extent to which any such factors might be involved, a second series of experiments were performed in which irreversibility was allowed to develop and the cross-circulation procedure was begun only after the therapeutic transfusion was observed to have failed<sup>26</sup> In this second series the results were precisely the same as in the first Perfusion *via* the splenic vein results in recovery "taking-up"<sup>25</sup> disappears, blood pressure gradually returns to normal and all signs of a restored peripheral circulation become manifest Perfusion *via* a systemic vein produces no noticeable improvement and death occurs as rapidly as if no perfusion had been carried out *It follows that the liver can be repaired even after it has suffered extensive damage and that it is the organ directly responsible for failure of the peripheral circulatory apparatus in shock*

The therapeutic objective in irreversible shock then requires (1) a determination of the mechanism operating between the liver and the peripheral circulatory apparatus and (2) a closer analysis of the nature of the contribution by the donor animal

In respect to the first of these objectives we may postulate (a) the elaboration by the damaged liver of a toxin capable of paralyzing vascular tone or (b) the existence of a hormonal product of hepatic origin, normally available for the maintenance of vascular tone which, like hypertensinogen and fibrinogen, disappears as the hepatic cells become increasingly incompetent No evidence for the latter is yet available

That toxins can induce shock or increase susceptibility to shock is a well-recognized clinical fact, e.g., as in the case of infection Are there any endogenous toxins in shock in which an infectious process can be safely excluded?

Chambers and his collaborators<sup>27</sup> suggested the presence of a circulating toxin in hemorrhagic and tourniquet shock. Callicrein, which occurs in animal tissues, produces shock when injected in concentrated form<sup>28</sup>. But its spontaneous appearance in the blood during shock cannot be demonstrated. Prinzmetal and Bergman<sup>29</sup> believe that a toxin is present in the blood of rats immediately after producing a hot water burn. Shorr *et al*<sup>17</sup> developed the hypothesis that shock is due to an endogenous vasodepressor toxin by demonstrating a vasodepressor principle (VDM) in ice-cold saline washings of liver from the dog in hemorrhagic shock. Less is found in hepatic vein blood, still less in striated muscle and none elsewhere. This toxin of hepatic origin produces a transient shock-like state of peripheral flow in the mesentery of the test rat. If enough can be produced to permit testing its capacity to induce the shock state and to carry the latter to its lethal termination, stronger evidence of its specific etiology in shock would then be provided. We have reservations concerning the specific relation of this toxin to the shock state because it has not been found in dogs which were not under the influence of barbiturates. It is our view that the barbiturates intensify the shock state and so complicate the findings. Blood samples taken from our shocked animals (in which we used morphine only) and assayed for toxin in Shorr's laboratory did not show any parallelism between the clinical state of the animal and the toxin assay<sup>30</sup>. These tests, however, are yet in the exploratory stage. If a toxin is responsible for the lethal outcome of the shock state, it is difficult in our experiments to account for the healthy state of the donor animal when the recipient dies in shock. One must then assume a neutralizing function in the donor which is not available to the recipient in spite of a free intermixture of the two blood streams.

If the donor cures the recipient by neutralizing a toxin which acts on the peripheral vascular musculature, the same service should be available to the recipient regardless of the route of cross-circulation. Shorr states that the toxin from the shocked dog's liver is also formed by anoxic liver *in vitro* and is inactivated by healthy liver tissue. The toxin stops being elaborated if the anoxic liver is restored to an aerobic environment within a few hours. Since the donor makes a therapeutic contribution only because his arterial blood reaches the liver of the recipient directly, the donor's blood achieves its effect at least in large part by restoring an aerobic environment to the liver, rather than by the neutralization of a circulating toxin.

#### WORK<sup>†</sup> IN PROGRESS\*

The nature of the donor's contribution accordingly requires further analysis. This contribution might consist (1) solely in a flow of arterial blood to the liver to supplement the deficient volume of oxygenated blood which the animal itself is supplying or (2) in an essential biologic substance no longer elaborated by the dog in shock. It is also possible that both are needed to

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\* Recent experiments were done with the assistance of Dr. E. D. Frank and Dr. L. H. Manheimer.

facilitate regeneration of that liver function which is essential for sustaining peripheral vascular tone or if a toxin is involved, to inhibit toxin formation

An initial step in the solution of this problem was made by perfusing the liver of the dog in shock by a supplemental arterial supply from its own femoral artery instead of from a donor animal<sup>31</sup> The volume flow from the femoral artery to the splenic vein nearly equaled the volume flow that was supplied by a donor animal In a series of 15 such autoperfusion experiments the course of the shock state was definitely altered in that the rate of "taking-up" was reduced and survival of the animal prolonged, but recovery from the shock state was not effected, except in one instance The evidence indicates that supplementary portal flow of normally oxygenated blood was not the sole contribution of the donor animal

A series of liver perfusion experiments, in which a variable capacity pump supplied with a reservoir of fresh blood is used in place of the donor animal, is now being conducted From the evidence to date, which is still preliminary, it appears that this will also fail to effect recovery and that the donor animal seems to make a biological contribution in addition to that of merely supplying arterial blood to the liver For example, the donor supplies glucose, because the recipient's blood glucose level is maintained when cross-circulated with a healthy dog but not when autoperfusion is performed If glucose is added to the autoperfusion circuit, the blood glucose level may be maintained In any case, the addition of glucose does not alter the final result What other substances the donor's blood provides which the recipient's own blood does not, remains to be determined

In another series of experiments now in progress, liver perfusion from the shocked dog's own femoral artery is accompanied by cross-circulation between the donor and the systemic veins of the shocked dog To date, the results of this study indicate that the benefit conferred does not equal that of direct liver perfusion The possible adverse effect of the additional A-V shunt created will require further evaluation

A complicating factor of serious import in many of these experiments is the development of intraperitoneal bleeding of massive proportions, which results in loss of the animal before the result can be evaluated This bleeding is not due in most instances to technical errors or local trauma It is an expression of the shock phenomenon and deserves intensive investigation, since it is an even grosser manifestation of tissue disintegration than the more familiar one of hemorrhagic extravasation into the gut

We observed long ago that bleeding into the intestine in hemorrhagic shock is mild or insignificant until the irreversible stage is reached and then occurs only if transfusions are given It is a striking fact that liver perfusion from a donor reduces this complication, whereas other types of perfusion do not By the use of silicone-lined tubing we have been able to reduce the amount of heparin needed in these experiments to a trace, but without completely eliminating the intraperitoneal bleeding, particularly in dogs who have been allowed to deteriorate too extensively Therefore, although we may be able to omit

heparin entirely in future cross-circulation experiments, we cannot expect to avoid this complication. Meanwhile, in an attempt to explain the bleeding we have made the following observations: (1) the prothrombin time increases only slightly in advanced shock, (2) the coagulation time is not altered, (3) fibrinogen is not produced by the liver during shock, but some remains in the blood and more is added from transfused blood. Consequently, the hemorrhage is presumably not due to gross defects in the coagulation process, (4) the portal venous pressure is substantially elevated in shock after transfusion (even without added inflow from an arterial anastomosis).<sup>32</sup> The range of elevation is sufficient to produce hemorrhagic extravasation into the gut and the peritoneal cavity.<sup>31</sup> To what extent the hemoperitoneum is a manifestation of the failure of liver recovery or merely an unrelated complication which prevents recovery that might otherwise occur, remains to be determined.

#### SUMMARY

Cross-circulation of the liver of the dog in hemorrhagic shock with a healthy donor animal is the only effective therapeutic agent so far known for the treatment of hemorrhagic shock irreversible to transfusion. The nature of the donor's contribution consists in something in addition to merely oxygenated blood flowing into the liver. At present the problem is to determine what this additional service is.

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# THE REDISTRIBUTION OF BODY WATER AND THE FLUID THERAPY OF THE BURNED PATIENT\*\*†

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As knowledge of the physiologic alterations peculiar to the burned patient has unfolded in the past two decades, the concept of plasma volume deficit has become firmly entrenched as the central feature<sup>1, 2, 3</sup> Restoration of this volume towards normal, or prevention of its diminution, has become the prime objective of fluid therapy But burned patients still succumb to their injuries, and the frontier of survival has not been pushed very far back despite isolated reports of the survival of remarkably extensive burns<sup>4</sup> Apparently, there are still aspects of the disordered physiology of burns which we do not understand well enough to treat effectively The disordered fluid balance of burn shock may be confused by the presence of pulmonary damage or infection, by widespread physiologic changes due to the trauma, or to misdirected treatment

During a period of enthusiasm in the field of burn therapy, ranging from treatment with large quantities of sodium ion to massive whole blood transfusion, we have planned a study based not on theory but on observation of the physiologic variables The present paper deals with the disorders of fluid distribution encountered in 19 patients New concepts of guiding the fluid therapy of the extensively burned patient have emerged

## METHODS

### Measurement of the Body Fluid Spaces

*Plasma volume* has been measured by the dilution of Evans blue dye, as described by Gibson and Evelyn<sup>5</sup> In the study of burns several considerations are pertinent to this method A clear serum is necessary for colorimetry and cannot always be obtained Hemoglobin and bilirubin may both be present in the early phases Standard correction for these substances has not yielded satisfactory results in our hands During the period of maximal nutritional deficit and forced feeding, the 8- to 12-hour fast required for clear sera is not always advisable \*

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\* The use of the dye method of measuring plasma volume in burns has a theoretic inaccuracy which has been discussed elsewhere<sup>6</sup> The increased capillary permeability of the burn wound permits equilibration of the dye with a larger volume of fluid outside the capillary wall, but such equilibration requires time Practically, we have found by checking the dye method with the radioactive red cell volume<sup>7</sup> that if two readings are made after injection of the dye, the first at 10 and the second at 30 to 50 minutes after injection the determination is still valid even in the extensively burned patient

Normal values for the plasma volume (PV) are variable and occupy a range from 3.5 to 5.0 per cent of body weight, the latter figure being exceptional and found only in large healthy males of athletic habitus. For the average patient 3.5 to 4.5 per cent of body weight is a normal range, it will be noted that this involves a 30 per cent variation from the lower figure.

*Red cell volume* has been measured by calculation from the dye plasma volume and the large vessel hematocrit, and by the dilution of red cells containing radioactive iron, a method which is independent of hematocrit differences in various areas of the vascular bed. The radioactive method has been described by Gibson *et al.*,<sup>8, 9</sup> and the results in our patients are reported in the paper dealing with the anemia of burns.<sup>7</sup>

*Extracellular fluid volume* has been measured by the dilution of thiocyanate<sup>10, 11</sup> and of radiosodium<sup>12</sup> using the plasma concentration at 50 minutes after injection. The latter method is perhaps the more physiologic though they both readily reveal extracellular fluid expansion or contraction and in their similarity and occasional variance have yielded much data of interest in these patients. (In the tables the plasma, thiocyanate and radiosodium volumes are designated by PV, SCNV, and NA<sup>+</sup>V respectively.)

Our experience in measuring the body fluid spaces coincides with that of others in finding a wide variation in normal values for plasma volume, red cell volume and blood volume, furthermore, modes of expression such as "per cent of body weight," "cubic centimeters per kilogram," "liters per square meter," "cubic centimeter per centimeter of sitting height" and other more complex measurements yield little increase in accuracy or predictability<sup>13, 14, 15</sup>. For our purposes, "per cent of body weight" seems most practical, and normal values are as follows:

Plasma Volume	3.5 — 4.5 % BW (= Body Weight)
Dye Red Cell Volume	3.0 — 4.0 % BW
Radioactive Red Cell Volume	2.6 — 3.5 % BW
Thiocyanate Space	18.0 — 25.0 % BW
Sodium Space	18.0 — 25.0 % BW

### Measurement of External Wound Loss

By measuring the amount of sodium in the exudate, the external water loss from the wound may be calculated. The calculation is based on the assumption that sodium leaves the wound in the concentration found in plasma, a reasonable assumption since this concentration is found in bleb fluid. Methods based on the weight of dressings suffer from loss by evaporation, the nitrogen content is a poor guide to water content as the breakdown of protein to non-protein-nitrogen and the evolution of ammonia by bacterial putrefaction affect both calculation and result.

By calculations from water intake and output, with estimates of insensible water loss and measurements of extracellular space expansion, the water loss

through the wound may be further approximated. For example, if in a four-day period a patient is given 20,000 cc of water, and excretes 4,000 cc, undergoes an extracellular expansion of 5,000 cc and loses by lungs 1,000 cc a day for a total of 4,000 cc then

$$20,000 - [4,000 + 5,000 + (4 \times 1,000)] = 7,000 \text{ cc}$$

The 7,000 cc represent unaccounted for water loss and must have been either stored in cells or lost via exudate

*Measurement of hourly urine output* has been most helpful clinically in controlling therapy and casts considerable light on the renal mechanism in burns. This method will be described in detail later in this paper.

*Measurement of red cell, electrolyte and protein concentrations* in the blood have been carried out as a reference point for other calculations.

*Measurement of electrolyte and protein balances* including exudate losses, have been an integral part of the study and are described in a subsequent paper.<sup>16</sup>

#### OBSERVATIONS

The objective of the studies recorded in this paper has been a comprehensive plan for the fluid therapy of the extensively burned patient. The appraisal of the plan of therapy has depended not so much upon survival of the patient as upon the values obtained in a series of coordinated laboratory measurements. The maintenance of an adequate circulation has been judged not only by continuous measurement of the renal excretion of water and electrolytes but also by repeated direct determinations of the plasma and red cell volumes. The demands of the wound have been gauged by measuring both the expansion of the interstitial fluid space and the fluid, electrolyte and protein losses from the wound surface. The subsequent fate of the huge amounts of fluid given as therapy and pocketed as edema has also been studied by continuing the laboratory observations throughout the period of resorption of the wound edema. From the balance sheet the true needs of the patient have been reconstructed.

Observations have also been made of the size of the fluid spaces in healthy human beings under normal and induced circumstances and in patients with diseases either akin to burns or requiring therapy commonly employed in burned patients. Space does not permit inclusion of these control studies.

#### BURNED PATIENTS

Of the 19 patients included in this study 16 had extensive skin burns, covering from 25 to 85 per cent of the body surface, five of these patients died. The 17th patient had a burn of 15 per cent and the 18th and 19th burns of only 5 and 4 per cent. The 19th also had a pulmonary burn.

It was obviously necessary to have a plan of therapy with which to initiate the study, one elastic enough to be altered as knowledge was gained. Formulas for estimating the fluid requirements of a burned patient based upon the degree

of hemoconcentration had been recommended at the beginning of World War II. The hemoglobin concentration or hematocrit of peripheral blood was used to determine the degree of hemoconcentration<sup>17, 18, 19</sup>. For each degree of hemoconcentration present a certain volume of fluid was recommended as therapy. Adequate to restore to normal the volume of plasma circulating at the time the measurement was made, these formulas failed to take into account the volume of plasma fluid which was to be lost from the circulation in the hours after the particular hemoglobin or hematocrit reading had been made. Thus an extensively burned patient, seen within a half hour after injury when the hemoconcentration had had little time to advance, would be given a small quantity of fluid whereas in reality such a patient requires many liters of fluid in the first 12 hours in order to avoid circulatory insufficiency.

It was considered that a sounder prediction of the fluid requirement of the burned patient could be made on the basis of the extent of the surface area damaged.\* The reasoning took into account not only that the volume of plasma water lost from the damaged capillaries into the wound is proportional to the area of skin surface burned rather than to the depth of injury but also that planning of therapy for an entire 24- or 48-hour period was in order regardless of the degree of hemoconcentration at the particular moment the patient was seen<sup>20, 21</sup>.

Part of the program on burns undertaken at the Massachusetts General Hospital for the OSRD, was a study of the advantages and shortcomings of administering fluid in accordance with the extent of surface area damaged. The following formula for this relationship, based on experience with extensively burned patients treated in 1942-43, was adopted for trial<sup>22</sup>.

### Surface Area Formula for Fluid Therapy

The surface area formula for fluid therapy of burned patients is based upon the concepts that the demands of the wound are proportionate to its extent, that the rate of edema formation will decrease with time after injury and that the requirements of normal metabolism including kidney function, must be met in addition to those of the wound. In the average sized adult for each 1 per cent of the body surface burned, 75 cc of plasma and 75 cc of non-colloid-containing isotonic electrolyte fluid are given in the first 24 hours. These fluids are to fill the expanding spaces of the wound and to keep up with any seepage of the

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\* At a conference on burns called by the National Research Council on January 7, 1942, under the chairmanship of Dr. I. S. Ravdin, it was agreed that a surface area formula should be recommended to the Armed Services. This was the first time that the extent of the surface area burned was to be a major guide to the therapy of burn shock. Drawing on his experience with the hemoconcentration formulas and the surface area as a first-aid fluid formula, Dr. Henry N. Harkins calculated that patients with 10 per cent or more of their body surface burned should be given 1,000 cc of plasma intravenously in the first 24 hours for each 10 per cent of the surface burned. The conference recommended that salt solution, not to exceed the same quantity, should also be given. The formulas tested by us have been modifications of this recommendation.

wound surface The quantity of non-colloid electrolyte solution equal to the amount of plasma is planned because measurement of the fluid in burn blebs suggests that wound fluid has a protein concentration a half to two-thirds that of normal plasma but a pattern and concentration of electrolyte essentially that of plasma The electrolyte solution is to be given by mouth to those patients who are not nauseated, otherwise it is given intravenously along with the plasma The intravenous route is considered less desirable since it is theoretically possible that the more prompt dilution of the protein of the circulation occasioned by the intravenous injection accelerates capillary filtration and edema formation in the wound For the oral administration, an isotonic solution of sodium was prepared with one-third of the sodium as bicarbonate and two-thirds as chloride, it was flavored with fruit syrup For the intravenous administration, the physiologic sodium chloride solution available to the armed forces was used, recognizing that the chloride concentration was in excess of that in the extracellular fluid and that it might produce high chloride concentrations in the plasma

One-half of the calculated amount of plasma and electrolyte fluid is given in the first eight hours and the second half in the subsequent 16 hours, in this fashion adapting the rate of the therapy to the expected rate of transudation into the wound Both the experimental<sup>23</sup> and clinical observations carried out at this hospital suggest that the rate of edema formation follows a parabolic curve, rapid at the beginning, tapering off as wound pressure increases, with cessation of further edema formation around the 36th hour In keeping with this decreasing rate of edema formation, the plan includes for the second 24 hours a fluid ration equal to one-half that given in the first 24 hours

In addition to the above, 2,000 cc of fluid is given in each 24-hour period to maintain urine flow (Insensible water loss and the water resulting from metabolism were not specifically considered) The fluid is given preferably by mouth and consists of palatable liquids, those containing sugar and potassium, such as fresh fruit juices, being offered freely If the fluid has to be given intravenously, glucose in water is used The volumes of each of these three fluids are subject to alteration according to the exigencies of the case, the continued presence of hemoconcentration or cessation of renal output indicating the need for accelerated intake \*

### Wound Edema—Expansion and Contraction of Interstitial Space

The volume of wound edema, the rate of edema formation and its subsequent subsidence have been measured in 14 patients \*\* The volume of wound

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\* It should not be construed in the application of the formulas described in this paper that whole blood transfusion is contraindicated The need for whole blood is discussed in the paper dealing with the anemia of thermal burns <sup>7</sup>

\*\* The edema observed was not due to lack of pressure dressings To all burns of the head and extremities dressings of bulky, compressible cotton were applied and held firmly in place by elastic gauze bandages The pressure thus afforded reduced the edema locally but displaced it proximally The effect of pressure dressings and their limitation in sparing plasma loss are discussed elsewhere <sup>24</sup>

edema equals the increase in volume of the interstitial space over normal, the interstitial space being the extracellular fluid volume minus the plasma volume. Previous clinical observation of visible burn wounds not covered by bandages, such as those of the face, suggested that maximal edema in the human being is reached between the 36th and 48th hours and that in burns of partial thickness, the subsidence of the edema may be almost as rapid after the 48th hour as its formation. Care was therefore taken to make as many determinations of the extracellular space as practicable within the first few days, with always one determination close to the 48th hour. In this manner it was possible to test the clinical impression and determine the maximal volume and the rates of edema formation and disappearance. The results are divided according to both the extent and the depth of injury. Differences in value were found between the thiocyanate and radioactive sodium ion determinations in some patients during the phase of edema formation and during subsidence of edema in patients with extensive deep septic wounds. The data are given in Tables I-X. The relation of maximum edema reached as the result of the burn trauma to the extent of injury is depicted in Chart 1.

*Circumscribed Burns.* Fluid space measurements were carried out in two patients with circumscribed burns.

**Case 264 \***—A 41-year-old woman was admitted immediately after receiving circumscribed partial thickness burns of the arms, 5.5 per cent in extent.\*\* The interstitial space increased not more than one liter in volume, the variations both in thiocyanate and radio-sodium volumes are within those inherent in the methods (Table I, Chart 1). The plasma volume during the period of maximum edema was at the lower level of the normal range for women (slightly lower than that for men). The patient received no specific fluid therapy for her burns because of their limited extent. She showed no clinical evidence of systemic disturbance.

**Case 205**—In contrast to the findings in the previous case are those in a man of 56 years of age, with partial thickness skin burns of even lesser extent (4 per cent), limited to hands and face, but who also had a pulmonary tract burn from the inhalation of hot oil. The interstitial space expanded 7 liters in the first 48 hours (Table II, Chart 1). This expansion, out of proportion to the area of skin damaged and more like that encountered in the extensively burned, is believed due to the combination of the position of the skin burns which resulted in a greater spread of subcutaneous edema and of the pulmonary damage.

The interstitial space did not retract to normal until after the third week. On the 14th day the patient's plasma volume was excessive, a phlebotomy was followed promptly by clinical relief. This enlargement of both portions of the extracellular space is believed related to over-enthusiastic fluid therapy initiated after the 36th hour as well as to the pulmonary damage of which there were continuing signs and roentgenographic evidence.

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\* The same case numbers are used in all articles on burn patients studied at this hospital under contract with the Committee on Medical Research. Numbers 1 through 39 refer to the Cocoanut Grove fire cases, numbers 40 through 96 to cases studied before the Cocoanut Grove fire, and numbers 97 through 282 to cases studied since the Cocoanut Grove fire.

\*\* Extent of the burn, total, partial, and full thickness, is always expressed as per cent of the body surface in the papers of this series. The per cent is computed according to the Berkow scale.<sup>25</sup>

TABLE I  
PLASMA AND EXTRACELLULAR FLUID DATACase 264  
Female Age 41 Weight 52.5 Kg  
Extent of Burn 5.5 percent total 0 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc	% BW	cc	% BW	cc	% BW
2	1740	3.33	9,020	17.3	10,900	20.9
3	1790	3.42	11,700	22.4	10,790	20.6
8			10,300	19.8	11,900	22.7

TABLE II  
PLASMA AND EXTRACELLULAR FLUID DATACase 205  
Male Age 56 Weight 79 Kg  
Extent of Burn 4 percent total 0 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc	% BW	cc	% BW	cc	% BW
0(4.5 hrs)	2760	3.50	14,850	19.0	15,590	19.6
1					19,950	25.2
2					21,900	27.8
3					19,600	25.0
7	2720	3.45	21,500	27.2	22,300	28.4
9	3290	4.30	24,730	31.2	18,320	23.0
14	4250	5.30	19,400	24.5		
17					19,900	25.0
20	3670	4.65	23,270	29.2	20,000	25.3
26			17,260	21.8	18,200	23.0

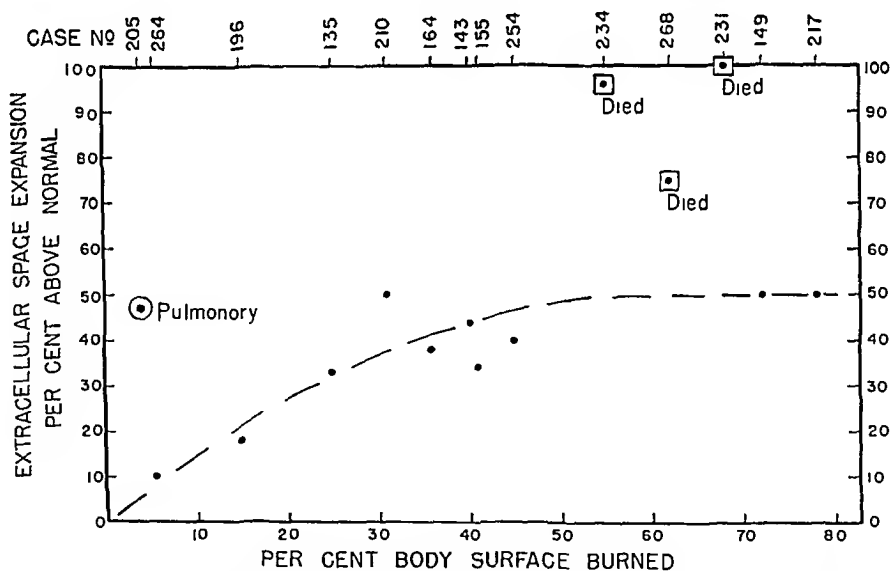


CHART I—Relation of Extent of Burn to Expansion of Extracellular Space and Need for Fluid Therapy

The extent of the burn wound in per cent of body surface damaged is plotted against the expansion of the extracellular space in per cent above the normal volume. The observation recorded is the maximum found from the 36th to 72nd hour in each of 14 patients.

The patient to whom each observation pertains is identified by the case number at the top of the chart. Three of the patients died (Cases 234, 268 and 231), the expansion was 75 per cent or greater. Of the 11 patients who survived, including the two most extensively burned, none had an expansion greater than 50 per cent. One of the survivors (Case 205) had an expansion out of proportion to the extent of the skin burn (4 per cent), he had inhaled hot oil.

*Extensive Burns* The expansion and contraction of wound edema were studied in 12 extensively burned patients. In eight the fluid therapy is considered to have been adequate, in two it was excessive, one of the patients succumbed. In the remaining two, it is probable that poor kidneys and infection rather than excessive therapy produced an inordinate expansion of the interstitial space and eventual death.

Of the eight patients receiving adequate but not excessive therapy, five are considered together because they were consecutively treated patients with extensive full thickness burns upon whom comparable studies were made.

**Cases 135, 143, 149, 155, 164.** The measurement of the dye plasma and thiocyanate volumes were planned with the specific purpose of plotting both the rates of edema formation and retraction. Multiple measurements were made in the first seven days and occasionally thereafter. The data are summarized in Table III and Charts 2a, b and c (See also Chart 1).

The patients were fully grown, their ages varying from 16 to 48 years. In Table III, Column 3, it is seen that the burns ranged in extent from 25 to 72 per cent. The extent of full thickness destruction was also variable, from 7 to 38 per cent. Column 5 indicates that immediately following admission the patients showed hemoconcentration both of cells and protein. In Column 9 are shown the increases found in the thiocyanate space. The increases average 8 per cent of the patient's body weight, varying from 7 to 11 per cent. These increases represent expansions of 35 to 55 per cent over the normal extracellular volume. In Column 10 it will be noted that the total therapy administered to the patients in the first 48 hours averaged 328 cc per per cent of burn. Of the figures in this Table, the deviation from the average is the least and for the reason that the therapy given each patient was almost exactly that outlined by the surface area formula. For anyone not familiar with the treatment of burns, this amount of fluid may seem remarkably large.

In Column 11 it will be noted that the plasma given in the first 48 hours averaged 92 cc per 1 per cent burn. The amount of plasma given per per cent of burn varied more than did the total amount of fluid. The amount outlined in the formula is 110.5 cc per per cent burned and it was exceeded only in the most extensively burned patient. In the others when the plasma ran slowly through the needle, the deficit was replaced by salt solution.

In Column 12 it will be noted that, with the exception of the most extensively burned patient, the thiocyanate space expansion was slightly larger than the amount of plasma given.

Column 13 indicates that the urinary volume in all of the patients was adequate and approached an excessive amount in only one. Case 143.

The importance of renal function as an indication of the state of the circulation and of hydration is illustrated by the following experience with Case 149, the most extensively burned. An indwelling catheter had been secured in the patient's bladder at the time of entry to the hospital and the urinary output was carefully observed. In the 7th hour after injury the flow of urine ceased. A second intravenous needle was inserted and plasma was pumped by syringe into



TABLE III  
SUMMARY OF BODY FLUID MEASUREMENTS AND EARLY THERAPY IN FIVE SEVERELY BURNED PATIENTS

1	2	3	4	5	6	7	8	9	10
Pts	Wt	Percent Burn	Admission Hours Post-Burn	Hemoconcentration Maximum Hematocrit and Protein	Admission PV	Admission SCNV	48-Hour SCNV	To SCNV Increase	Total Therapy 1st 48 Hrs
No	Kg	Total/Full Thickness	Hrs	Percent Cells Gm/100 cc	cc	% BW	cc	% BW	cc
135	53 0	25/15	5 0	50 0	1880	3 55	14,100	26 7	8 600
143	58 7	40/34	1 0	56 4	(Footnote 1)	(Footnote 1)	16 900	29 0	12 000
149	66 1	72/38	1 5	70 0	1940	2 90	22 660	34 0	21 375
155	78 2	41/26	4 0	58 0	(Footnote 1)	(Footnote 1)	20 970	27 0	16 100
164	71 2	36/7	0 5	50 7	2840	4 00	19,070	27 8	11 107
Averages				57 0			18,740	28 7	13 836

11

12

13

14

Total Plasma 1st 48 Hrs	Plasma Given SCNV Expansion	Urine Output 1st 48 Hrs	Calculated External <sup>1</sup> Water Loss <sup>4</sup> 1st 48 Hrs
cc	cc	cc	cc
2250	90 0	1440	1860
4250	106 0	5900	0
9250	129 0	4450	7465
3250	79 2	0 592	5270
2071	57 5	0 370	0
4214	92 3	3854	0
		160 cc/hr	

<sup>1</sup> These determinations could not be completed because of extensive hemolysis producing free serum hemoglobin

<sup>2</sup> This thiocyanate volume was not done on admission, but was done about three hours after admission after treatment had been under way for about two hours. It therefore represents a considerably expanded value over normal

<sup>3</sup> This calculation of increase in thiocyanate space is based on an increase over the normal estimated value for this patient rather than an increase over his first observed thiocyanate volume

<sup>4</sup> Calculation of external water loss Ext Loss = Total Therapy—(SCNV Expansion + Urine + 2000 Insensible Loss)

both veins, 750 cc of plasma being injected in the space of 20 minutes. Ten minutes after the start of this accelerated plasma injection, urine once more dripped from the catheter. An hematocrit taken at the start of the accelerated injection proved to be 70 per cent, and that an hour later was 63 per cent. Had the catheter not been in place, the cessation of renal function and the circulatory insufficiency producing it, would certainly not have been so promptly recognized. Although the period of anoxia necessary to damage the kidney has not been established with certainty in the human being,<sup>26</sup> it is probable that had the deficient circulation to the kidney persisted for a matter of hours, sufficient renal damage would have accrued to jeopardize the survival of the patient. This episode dramatically illustrates the usefulness of a close observation of renal output in managing fluid therapy in the early phase of an extensively burned patient. Only by dint of this rapid massive therapy was a fatal outcome avoided and when the opportunity to mobilize his edema arrived he excreted 20,000 cc of urine in four days (second to sixth days). A young male, he was able to excrete this large amount of water, whereas an older patient might not have been able to do so and would have been more prone to develop visceral and pulmonary edema during resorption. Since the treatment administered was barely enough to avoid serious hemoconcentration, the edema and subsequent diuresis cannot be regarded as due to over-zealous treatment.

In Column 14 it will be observed that the calculated external water loss is extremely variable. Though it is accepted that some patients with dry, charred, parchment-like burns may have little or no external water loss in the first 48 hours (Case 143 had burns of such character), this was not so true of Case 164. One cannot, therefore, accept the zero figures as absolute, but rather as a general indication that external water loss was minor. In patients 155 and 149, external water loss was large by this type of derived calculation, both patients had large areas of moist wounds.

The rate of edema formation is illustrated in Chart 2a. The figures charted are the per cent deviation from the normal thiocyanate space, since the variations of plasma volume were inconsequential, the changes depicted represent changes in the interstitial space. The increase in volume of the interstitial space is rapid in the first 48 hours, the maximum volume measured in four patients being between the 40th and 50th hours. In three of these patients the next measurement, made between the 5th and 6th days and before any operation, showed the volume to have decreased (Cases 135, 143 and 149). In the 4th (Case 155), the volume remained unchanged on the 5th day, because of the appearance of respiratory difficulty it is believed he may have been given an excess of fluid. The one patient whose interstitial fluid volume increased significantly after the 48th hour was Case 164. The measurement was made on the 7th day, two days after an excision and grafting operation, the red cell mass of 1,210 cc measured at the same time indicated a severe anemia. This continued increase in interstitial fluid volume doubtless had a complex origin and is presumably not a primary result of the burn. Observations on the control patients indicate that the operation and severe red cell depletion should be

associated with an increase, wound infection known to be present also presumably played a role

In summary, the findings depicted in Chart 2a indicate that the expansion of the interstitial space due to burn trauma occurs rapidly, reaching a maximum within 48 hours. Other factors such as wound infection, operation, anemia and excessive fluid therapy may influence the degree of expansion and time of onset of retraction

Charts 2b and c depict the variations encountered in concentration in the peripheral venous blood of protein and red cells in terms of the per cent deviation from normal. Of the protein there is an initial increase in concentration, the explanation of which is discussed in the paper on the shift of protein<sup>27</sup>. This increase is inversely proportional to the concentration of protein in the burn edema fluid. The increase is followed by a dilution with eventual return to normal with healing of the wounds. The extent and duration of the dilution

CHART 2a

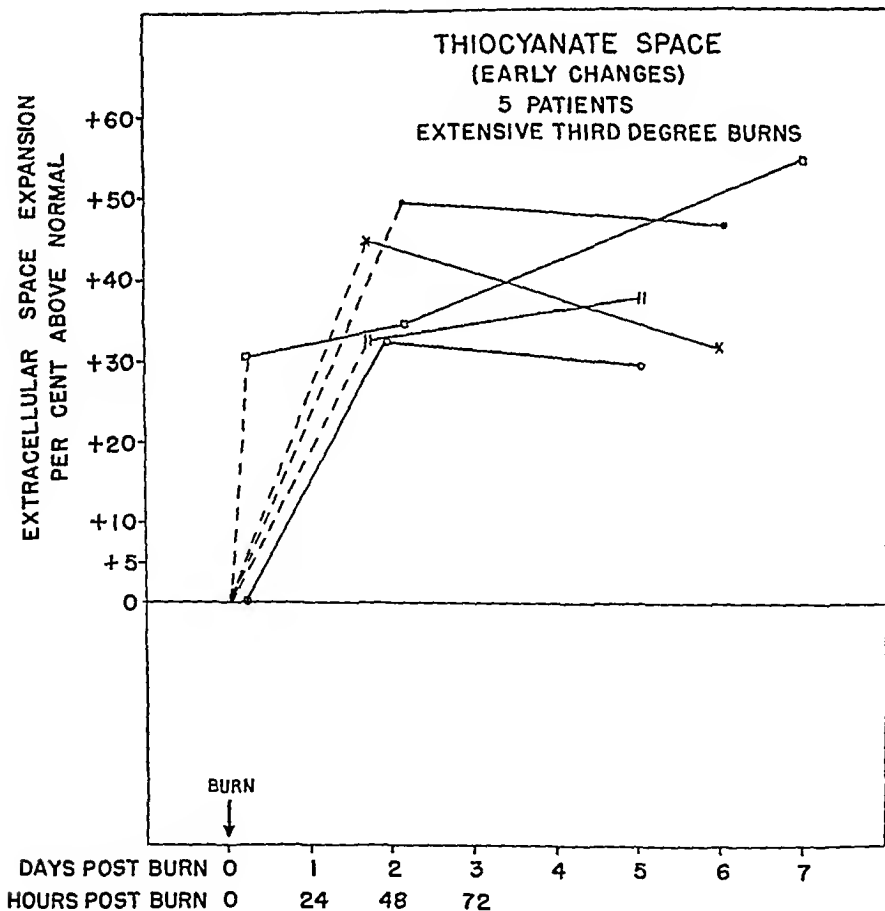


CHART 2a, b and c—Three charts demonstrating the early thiocyanate space changes and alterations in peripheral concentration of protein and red cells in the five severely burned patients tabulated in Table III (Cases 135, 143, 149, 155 and 164). For discussion see text

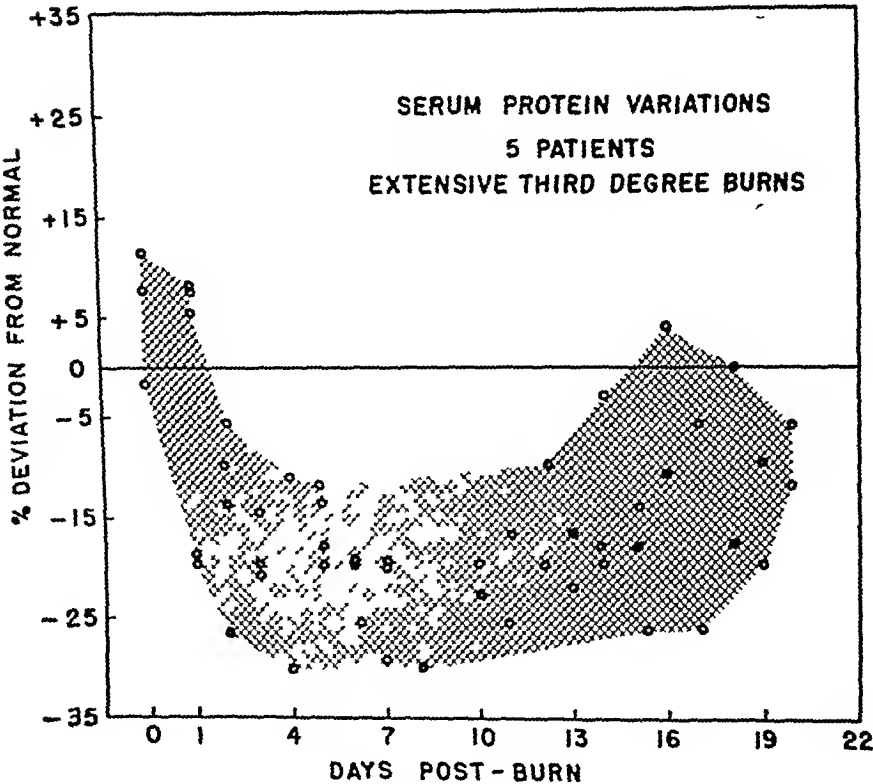


CHART 2b—(See legend under Chart 2a)

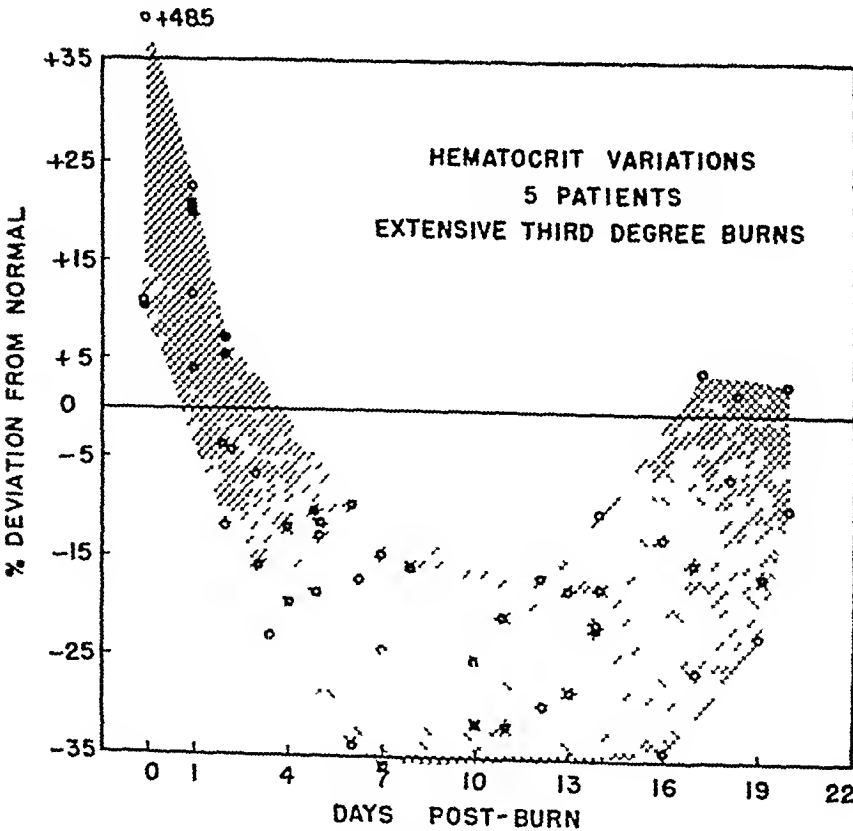


CHART 2c—(See legend under Chart 2a)

depends upon the osmotic balance left by fluid therapy, resorption of edema fluid, kidney function, protein destruction and synthesis

The graph of the concentration of red cells (Chart 2c) follows a curve parallel to that of the protein, the initial concentration resulting from loss of plasma volume, and the subsequent dilution resulting more from diminution of red cell mass than from excessive plasma volume in these cases<sup>7</sup>

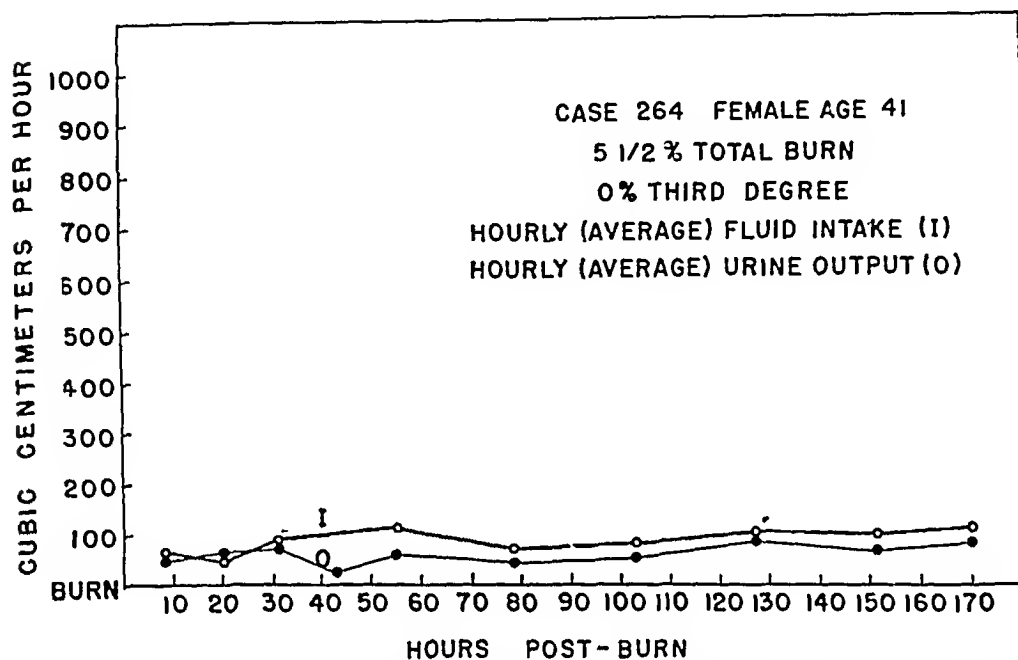


CHART 3—Intake-Output Chart of a Patient with a Circumscribed Burn (Case 264)

The intake-output charts are plotted similarly. The ordinate depicts the fluid intake or output rate in cubic centimeters per hour, the abscissa hours after the burn. Intake is indicated by I, output by O. Volumes indicated by points at 12- to 24-hour intervals are averages. The actual observed hourly renal outputs from an indwelling catheter are indicated by multiple, closely spaced points.

In Chart 3 there is no significant spread between the intake and output over that which would be produced by ordinary insensible loss.

In subsequent charts, as the intake progressively rises over the output following more extensive burns, the area intervening between intake and output is a function of the water stored in the wound and lost through the dressing.

The deep wounds of the five patients were treated with early excision and grafting, the initial operation taking place between the 5th and 7th days. Although there was a diuresis after the 48th hour, the interstitial space expansion persisted and final retraction to normal did not occur until healing of the wounds was well advanced. The patients were discharged home from the 60th to 122nd post-burn day with wounds healed.

In the 6th extensively burned patient who received adequate therapy, the findings are much the same as in the previous five cases with the addition that the extracellular space was measured with radiosodium as well as thiocyanate.

**Case 210**—A 34-year-old housewife was admitted shortly after receiving a 31 per cent total, 25 per cent full thickness burn. Her early course was marked by what was regarded

at that time as oliguria (see below), on her 6th day she had a saphenous vein ligation because of phlebitis following cannulation. On her 8th day she had an excision of a portion of her burns. These areas were partially grafted 11 days later, the patient had a long and difficult convalescence and was discharged home on the 128th post-burn day.

The observations made on this patient prove that the expansion of the interstitial space is obligate, not a result of therapy. On admission the patient showed a diminished plasma volume (Table IV) and this together with her high hematocrit and high protein concentration indicated the familiar early tendency to plasma loss and burn shock. An expansion of the extracellular space to 50 per cent above normal was observed.

The patient's initial treatment was not excessive and during the initial 48 hours the patient's urine output was at low but adequate levels, 1,470 cc during the first 24 hours (an average of 61 cc per hour) and 846 cc during the second (an average of 35 cc per

TABLE IV  
PLASMA AND EXTRACELLULAR FLUID DATA

Case 210						
Female, Age 34, Weight 73.0 Kg						
Extent of Burn 31 percent total 25 percent full thickness						
Day Post-Burn	PV		SCNV		Na*V	
	cc	% BW	cc	% BW	cc	% BW
0 (2 hrs)	1790	2.5	12,900	17.7	16,070	22.8
5	(1640)	2.3	22,200	30.5	21,600	29.6
8	3450	4.7	25,400	35.0	20,500	28.0
15	3330	4.6	20,300	28.0	19,600	27.0
24	2640	3.5	17,300	23.6		
32	2180	3.0	21,200	29.0	18,200	25.0
47	3040	4.2	21,200	29.0	17,900	24.5
61	3100	4.3	21,300	29.4	17,800	24.5
83	2620	3.6	16,900	23.1		
114	2460	3.4	20,400	27.8	18,500	25.3
127			17,500	24.0	16,900	23.2

hour). During the first 48 hours the patient received 11,253 cc of fluid of which 4,020 cc was plasma. According to the surface area formula described, her therapy for the first 48 hours was to have totaled 3,485 cc of plasma, a like amount of non-colloid-containing electrolyte solution plus 4,000 cc of fluids, a total of 10,970 cc. Although it is conceivable that her minimal requirement was less than given, this is unlikely in view of the continuing mild hemoconcentration and small urinary volume during the first 48 hours. It is of interest that the 8 liter expansion in extracellular fluid revealed by the second measurement (5 days post-burn) correlated so closely with the difference between intake and output during the first 48 hours, 8,937 cc (Chart 1). In patients who are flooded with water one cannot estimate the volume of the burn edema by the volume of fluid retained because the factor of renal function looms so large and a discrepancy between intake and output may reflect renal damage.

After the first 2 days, the patient's fluid therapy was intensified because the urine output was not at that time regarded as adequate. The intensified therapy consisted of approximately 19,000 cc of fluid during the next 3 days and the concomitant excretion of 12 liters of urine from the 3rd to 5th days, inclusively.

The remaining two of the eight patients with extensive burns receiving adequate therapy had burns of but partial thickness with only small areas of full thickness destruction.

**Case 196**—A male, age 51, received a burn of 15 per cent total, 1 per cent full thickness. His fluid therapy was purposely delayed until the 6th hour to permit study of the differential sodium-thiocyanate expansion in an untreated burn. At the end of five hours the thiocyanate space was only slightly higher than normal, 22.6 per cent of his body weight, whereas the sodium space, at 29.4 per cent, had expanded significantly (Table V).

TABLE V  
PLASMA AND EXTRACELLULAR FLUID DATA

Case 196  
Male, Age 51, Weight 80 Kg  
Extent of Burn 15 percent total 1 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc	% BW	cc	% BW	cc	% BW
0 (5 hrs)	3500	4.38	18,200	22.6	23,700	29.4
3			18,600	23.5		
4			17,250	21.6	16,050	20.0
9	4560	5.60	16,800	21.0	18,250	22.6

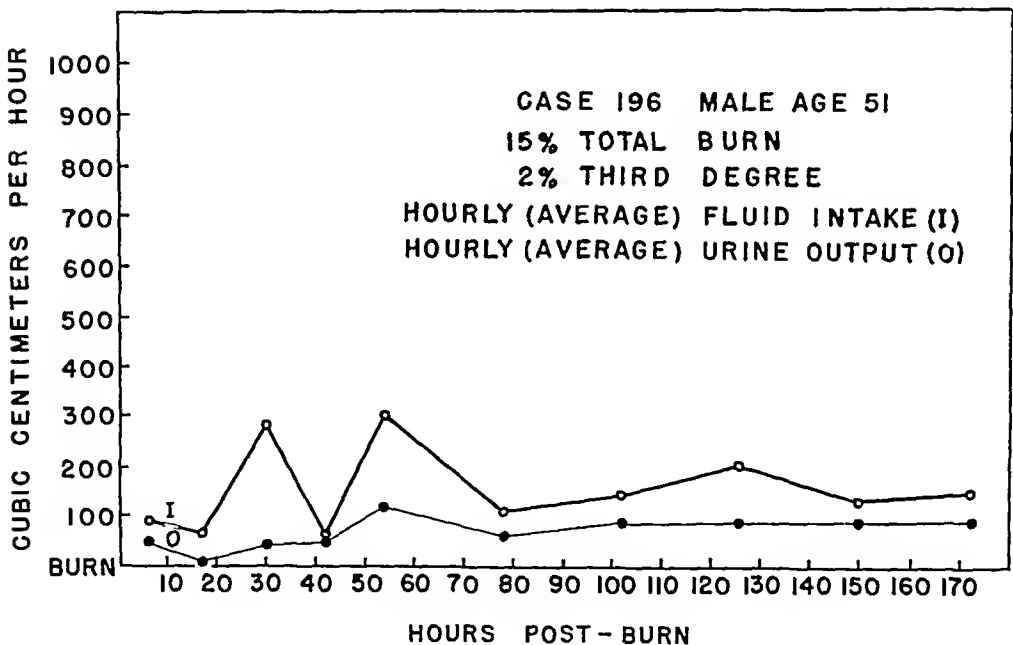


CHART 4—Intake-Output Chart of a Patient with a Superficial Burn of 15 Per Cent and a Full Thickness Burn of but 2 Per Cent (Case 196)

In this patient, slightly more extensively burned than that of Chart 3, the intake departs from the output during the first 60 hours, indicating some storage of water in the wounds. The discrepancy is less than that found in more extensively burned patients.

This finding of a larger sodium space is of interest because it has been observed in other patients within the first days after injury. It indicates that the volume of fluid in which sodium is dissolved is greater than that into which the thiocyanate can pass. Normally the volumes receiving these two ions are equal. This finding in burned patients suggests that the sodium ion penetrates

cell barriers not open to the thiocyanate and may be due either to the trauma *per se* or to a generalized dehydration in the acute phase after injury. The more prolonged elevations of the thiocyanate space frequently observed in patients with a chronic open wound (when the sodium space may be normal or near normal) also indicate some difference in significance of the two methods.

Case 196 never approached shock and never showed evidence of serious fluid disorder. The fluid allotment provided by the surface area formula proved adequate (Chart 1). He developed considerable facial and head edema, but by the 3rd day after his burn when his sodium space had returned towards normal, the patient had mobilized and excreted his edema and was essentially

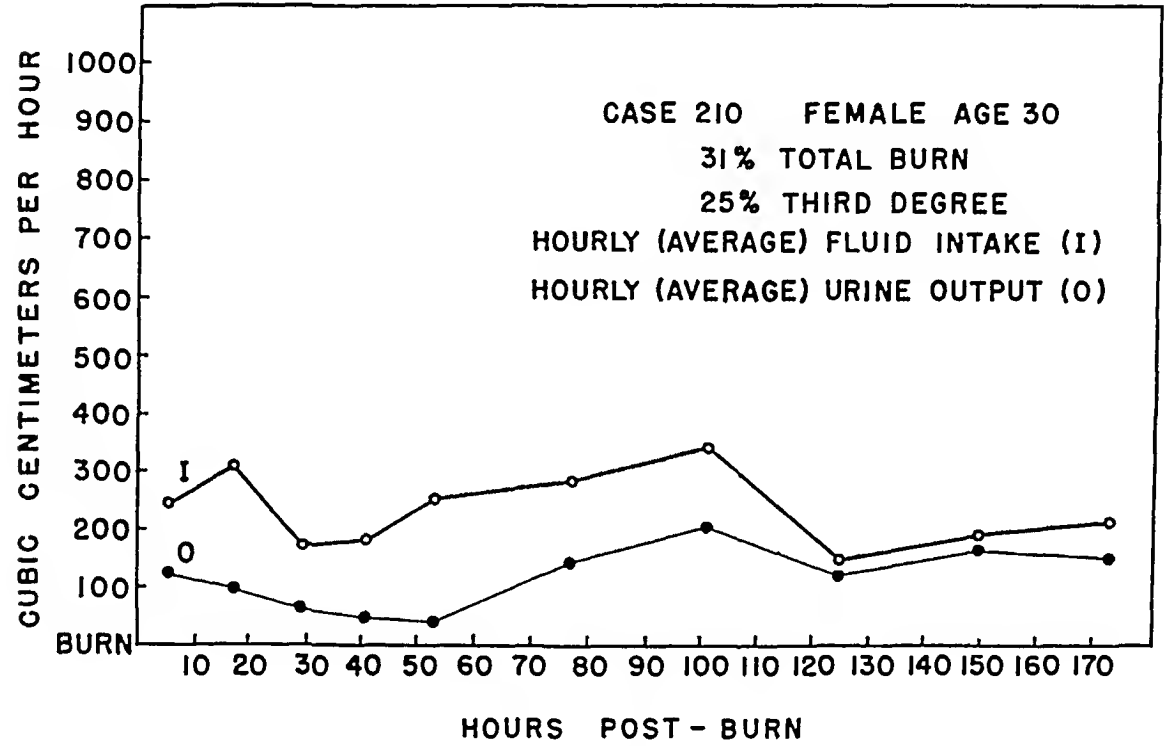


CHART 5 —Intake-Output Chart of a Patient with a 31 Per Cent Total Burn, Most of Which Was of Full Thickness Destruction (Case 210)

There is a prolonged discrepancy between intake and output which does not resolve itself until approximately 120 hours after the burn. During this time the patient was treated conservatively, at times her urine output being low. This may account for the prolonged period of intake-output discrepancy. The patient was slow to mobilize the edema fluid and did not show a clear-cut diuresis.

normal. His partial thickness burn healed with rapidity and he did not show the prolonged elevation of the thiocyanate space we have found associated with extensive, chronically infected, full thickness burn wounds. The changes indicate a need for water, electrolyte and protein adequate to meet the demands of the burn wound. These demands are transient as the tissues retain the viability essential to early recovery of capillary permeability and resorption, or mobilization, of the edema fluid.

This patient never demonstrated any hypoproteinemia, on two observations on his first post-burn day he showed slight hemoconcentration with respect to



red cells, presumably related to the accumulation of edema during that period and to the fact that treatment was purposely withheld for six hours to study the sodium-thiocyanate discrepancy

**Case 254**—A previously vigorous electric power linesman 38 years of age received an electric flash burn of 45 per cent, only 5 per cent being full thickness injury. Of note was the observation that the volume of his extracellular space when first measured was out of all proportion to the fluids which had been given him, and that he proved subsequently, nine months after the accident, to have an unprecedentedly large interstitial fluid volume as measured by dilution of the thiocyanate ion (Table VI).

According to the surface area formula, 3,375 cc of plasma and 8,750 cc of total fluids should have sufficed for his requirements for the first 24 hours. Because of continued

TABLE VI  
PLASMA AND EXTRACELLULAR FLUID DATA  
Case 254  
Male Age 38 Weight 68.8 Kg  
Extent of Burn 45 percent total 5 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc	% BW	cc	% BW	cc	% BW
2			35 000	51.0	26 500	37.0
3			29 600	43.0		
4			30 600	44.5		
5					27,700	40.0
7	4640	6.7	33,200	48.0		
11	4320	6.3	24 500	35.5	17 840	15.8
9 mos	3540	5.2	25 400	36.5		

apparent hemoconcentration of mild degree, judged by an hematocrit above 45 and a serum protein concentration above 7.0 Gm/100 cc, this allotment was exceeded by 750 cc of plasma and the total by nearly 3 liters of fluid in the first 24 hours. After his wounds were healed and he was clinically well, his hematocrit was found to be 47 per cent and serum protein 6.6 Gm/100 cc. In retrospect the fact that he secreted 2,538 cc of urine in the initial 24 hours, approximately 1,300 cc more than adequate, suggests that the urinary output would have been a wiser guide to the fluid therapy than the apparent hemoconcentration.

Measurement of the extracellular space by the thiocyanate method on the second day after the burn yielded a surprising volume equal to 51 per cent of the body weight. (The sodium space was significantly smaller.) Other patients showing a volume of such proportion were precariously ill and subsequently succumbed, yet this patient was clinically tolerating his injuries well. This paradox was explained when nine months later his extracellular fluid volume was found to be 36.5 per cent of his body weight. Such a large volume is unprecedented in our experience in an overtly healthy man, and remains unexplained.

If the volume of his extracellular fluid measured nine months post-burn is accepted as his normal, two concepts emerge which are useful in treating this type and size of burn. The increase in volume as a result of the burns found at 48 hours after burning, represents a 40 per cent increase in volume, not 150 per cent, above the normal (Chart 1), this change in volume in the first 48 hours would also represent a 10,000 cc increase, a figure in keeping with the actual fluid balance (including a 750 cc loss from the wound in the first 48

hours calculated from the sodium content of the exudate) A 40 per cent increase in extracellular volume is to be expected in patients with burns of this extent, comparable to the experience in patients with full thickness burns.

The second important finding is that the initially expanded interstitial space had retracted to normal by the 11th post-burn day Such a prompt retraction is not seen in patients with extensive skin burns predominantly of full thickness destruction

The experience with the two patients having extensive burns who received excessive fluid therapy and one of whom died is as follows

Case 217.—A 26-year-old woman was brought to the hospital within an hour after receiving burns of 78 per cent, 45 per cent of the total surface being of full thickness destruction Her first days were marked by intensive fluid therapy and massive edema

TABLE VII  
PLASMA AND EXTRACELLULAR FLUID DATA  
Case 217  
Female, Age 26, Weight 92.8 Kg  
Extent of Burn 78 percent, 45 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc	% BW	cc	% BW	cc	% BW
0 (1 hr)	2320	2.5	18,000	19.5	19,800	21.5
1			23,300	25.2	25,450	27.5
2					28,000	30.5
3	2890	3.1	27,500	30.0	22,800	24.7
10	4080	4.4	27,400	30.0		
24	4040	4.4	27,200	29.3	21,500	23.5
48	3880	4.2	28,800	32.0	19,600	21.3
68	3210	3.5	20,400	22.0	15,900	17.2
95	2970	3.2	26,400	28.6	20,100	22.0
13 mos	2400	3.2	19,600	26.0		(Wt 76 Kg)

From the 4th to 10th days she exhibited an increasing fever Because of this indication of acute infection, plans for early surgical care of her full thickness burns were abandoned Her wounds healed by granulation, epithelization and grafting over a period of many months She was discharged home on the 190th post-burn day

The first determinations of the plasma volume and hematocrit made one hour after injury indicated that an uncompensated plasma loss had already occurred (Table VII) The extracellular measurements made at the same time were within the normal range and suggested that the uncompensated plasma deficit and wound edema had resulted in some dehydration of the rest of the body As in other patients in the presence of dehydration, the radio-sodium volume was larger than that of the thiocyanate

Soon after therapy was begun the usual expansion of the interstitial space took place (Chart 1) By the 3rd post-burn day when the patient's clinical edema was beginning to subside, the sodium space receded back to 25 per cent of the patient's body weight and from then until healing the thiocyanate space remained expanded, the sodium space remaining more nearly normal This continued enlargement of the thiocyanate space but not that of the sodium, is the characteristic finding during the convalescence of patients with an extensive infected open wound

The patient's blood volume on the 3rd post-burn day was only 4.65 per cent of the body weight, one of the lowest total blood volumes we have observed in this group of cases and due unquestionably not only to the uncompensated plasma loss but also to massive destruction of red cells described in the report of the anemia of deep burns.<sup>7</sup>

In this patient, therapy based on the surface area formula would have resulted in the administration of 5,850 cc of plasma, a like amount of non-colloid-containing electrolyte solution, plus 2,000 cc of fluid, all in the first 24 hours. This schema was exceeded by 7,600 cc, for during the first 24 hours the patient received 21,313 cc of treatment of which 6,240 cc was plasma.

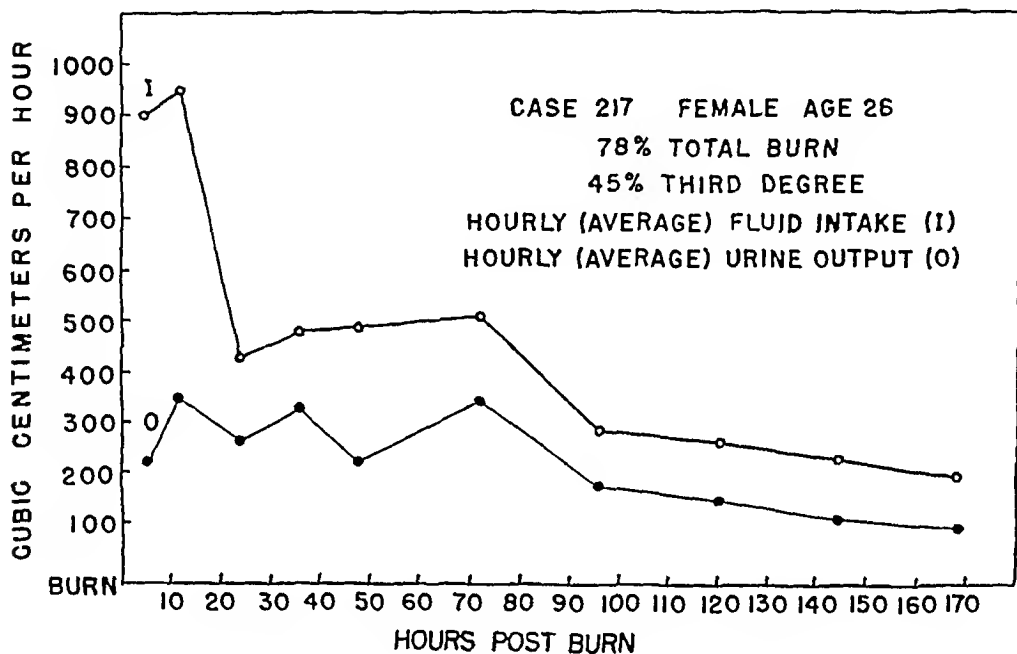


CHART 6—Intake-Output Chart of an Extensively and Deeply Burned Patient Whose Initial Treatment was in Excess of that Necessary (Case 217)

There is a large discrepancy between intake and output during the first 24 hours when edema formation is most rapid. From the 100th hour on, a normal relationship is exhibited. The high average urine output during the first 80 hours, averaging around 300 cc per hour, illustrates, in the light of subsequent experience, that fluid therapy was being administered at a rate more rapid than essential.

During this time the patient's urine output was 6,855 cc with an added 1,000 cc loss as vomitus. External losses arrived at by calculation were very severe amounting to somewhat over 5 liters during the first 48 hours.

This patient was treated with excessive zeal and the load placed on her kidneys thereby was tremendous. As it turned out, the volume of fluid indicated by the surface area formula should have proven adequate to the need, the forcing of the fluid intake might well have led to a fatality. During the patient's second 12 hours in the hospital she excreted 5 liters of urine and during the second 24 hours, 6,245 cc. This patient was fortunate in having a renal mechanism which could handle this load, in an older individual, visceral edema and cardiac decompensation would doubtless have occurred. By the end of 48

hours the patient was waterlogged and well into a period of water retention. She was clinically edematous with a sodium space of 30 per cent of her body weight, hematocrit of 33 and serum protein of 5.2 Gm/100 cc. were further evidences of this dilution. On the third day after the burn she excreted 8,215 cc of urine in a 24-hour period, an amount larger by 33 per cent than any 24 hour urine output during her entire stay, her edema decreased perceptibly, and the sodium space decreased 6 liters. This can be interpreted only as a spontaneous diuresis of retained water and its occurrence (often discernible only by careful intake-output data) constitutes the best possible prognostic sign from the point of view of fluid therapy in a severely burned patient, though it is not necessarily a portent of survival (cf. Case 268).

In summary this severely burned patient was given intensive fluid therapy, 7 liters more than that outlined on the basis of the extent of her burn. The patient survived because she did not have a primary lung injury producing increased pulmonary capillary permeability and edema, and because she possessed kidneys which could excrete as much as 8 liters of urine in a 24-hour period when called upon to do so by the resorption of the burn edema. It is possible that the patient needed actually less fluid than that outlined by the surface area formula because the excessive therapy may have distended the interstitial space even further.\*

TABLE VIII

## PLASMA AND EXTRACELLULAR FLUID DATA

## Case 231

Male, Age 36 Weight 70 Kg

Extent of Burn 68 percent total 39 percent full thickness

Day Post-Burn	PV		SCNV		Na*V	
	cc	% BW	cc	% BW	cc	% BW
1			32 700	46.5	29 300	41.9
2			27 000	38.5	28,900	41.3
3	3580	5.1	35 000	50.0		

**Case 231**—A 36-year-old male was admitted with burns of 68 per cent total and 39 per cent full thickness. Therapy was administered with great energy in an attempt to avoid shock and oliguria. On the second day post-burn the patient was seen to have massive edematous collections of fluid in his scrotum, buttocks and thighs. On admission he had shown burns of the nares and pharynx and by his second day, frank pulmonary edema was present and the patient was cyanotic. On the third post-burn day a tracheotomy was done in the hope of improving his oxygen exchange. After this the patient regained consciousness only fitfully and died on the 6th day.

During the first 48 hours in the hospital this patient received 32,645 cc of treatment of which 10,747 or roughly 30 per cent was plasma. This amount of plasma is equal to approximately 20 per cent of his body weight and was over four times his normal circulating plasma volume. It is about 35 per cent more plasma than the volume outlined by the surface area formula. During this time the patient excreted approximately 8 liters of urine leaving him with

\* In the experimental animal, the wound volume created by the burn may be slightly increased by an intravenous injection of isotonic sodium solution.<sup>23</sup>

an apparent water retention of about 24 liters. His sodium space expanded to 42 per cent of his body weight and his final thiocyanate space measurement was 50 per cent of his body weight (Table VIII, Chart 1). Too exact an interpretation of such data is not justified but since the expansion was measured at a time when there was generalized edema, the expansion presumably represents a widespread, massive disorder of fluid distribution and perhaps of cell permeability.

At times during the first 48 hours the patient excreted over 900 cc of urine per hour and the total urine output for the first 24-hour period was 5,671 cc

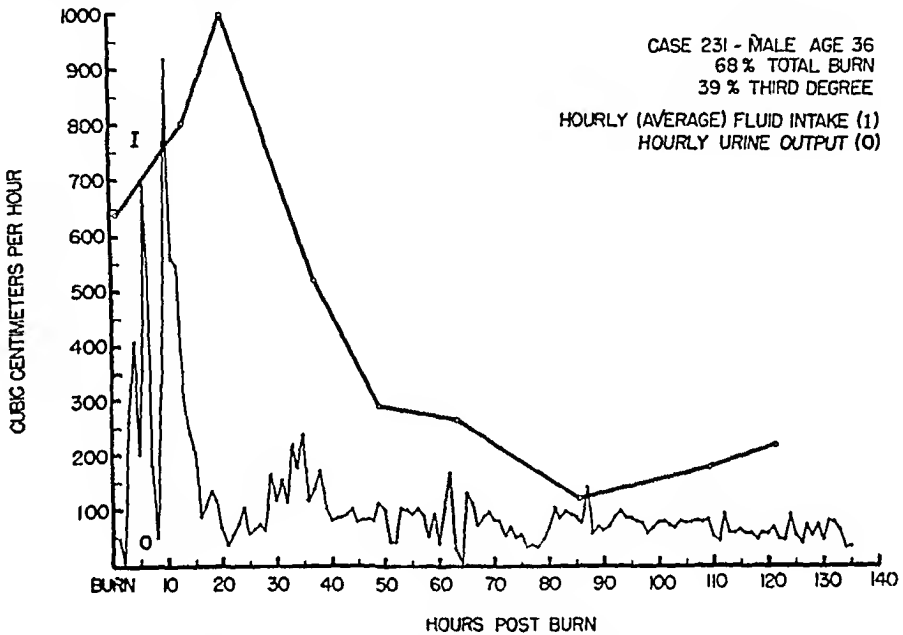


CHART 7—Intake-Output Chart of an Extensively Burned Patient Who Received Excessive Therapy and Who Succumbed (Case 231)

Early therapy was administered to the extent of a high urinary output during the first 12 hours. Despite the high output the fluid therapy was further increased until, during the period between 24 and 36 hours, the patient was receiving therapy at a rate approximating 1,000 cc per hour. Kidney function was unable to keep pace with this tremendous fluid load and the patient developed massive peripheral and pulmonary edema. Therapy was drastically cut at the 40th hour but the patient was unable to diurese the fluid already absorbed and succumbed at the 135th hour.

This output indicates that the patient was being subjected to a water load disproportionate to the actual requirement. However unlike Case 217, who could excrete large volumes of urine consistently for many days, this patient was unable to tolerate so much fluid. His kidneys could not keep up with the therapeutic infusions, the patient never showed any spontaneous diuresis. A direct injury of his pulmonary tract favored the development of intractable pulmonary edema, and death resulted.

In summary, although this patient's therapy was originally outlined on the basis of surface extent injured, the estimate of therapeutic requirement was greatly exceeded because of a clinical impression of the patient's tendency to shock. Huge quantities of fluid were given, the renal mechanism became over-

taxed although the kidneys of this healthy young male were presumably normal prior to burn. The inordinate expansion of extracellular volume was presumably as much the result of excess therapy as of the extensive burn itself.

The events in these last two cases lead to the realization that although patients with extensive burns require massive amounts of fluid therapy in order to compensate for the wound edema, there is a limit to the distensibility of the interstitial space compatible with life. In the first patient, the measured distention of the extracellular fluid volume did not exceed 50 per cent of the normal (Chart 1), the patient survived. In the second patient, the measured distention reached 100 per cent above the normal, the patient died. The safeguard to fluid therapy suggested is that fluid should be restricted to an amount compatible with no more than a 50 per cent increase in the extracellular fluid volume.

The final two patients with extensive burns, both of whom died, are

**Case 234**—A 68-year-old man suffered extensive burns (55 per cent total, 45 per cent full thickness) which proved fatal in nine days. For the first week the patient remained rational. He did not develop visible edema in unburned areas nor did he have

TABLE IX  
PLASMA AND EXTRACELLULAR FLUID DATA

Case 234						
Male, Age 68, Weight 60.0 Kg						
Extent of Burn 55 percent total, 45 percent full thickness						
Day Post-Burn	PV		SCNV		Na*V	
	cc	% BW	cc	% BW	cc	% BW
0 (1 hr)			16,500	27.5	15,900	26.4
1	2930	4.9	20,800	35.0	18,000	30.0
2			23,300	39.0	20,800	35.0
3	2350	4.0	28,800	49.0	19,900	33.0
4					24,300	39.0
5			24,800	42.0	20,600	34.5
6					19,450	32.5
7	3040	5.0	24,500	41.0		
8			28,800	48.0	11,260	18.7

pulmonary edema. In his last two days the patient failed gradually and succumbed with clinical evidence of bronchopneumonia and wound infection. Postmortem examination showed bronchopneumonia without alveolar edema, and a chronic nephrosclerosis long antedating the burn.

Fluid therapy was carried out with the intent of avoiding over-administration because of his age and the realization that cardiac decompensation would result if fluid therapy was not carefully restricted. The patient was given less sodium than had previously been the rule and whether as a result of this or of other factors the sodium space was throughout smaller than the thiocyanate space (Table IX). During the last days of his life his thiocyanate space was growing larger while his sodium space was decreasing. This discrepancy coexisted with increasing wound infection.

The patient's therapy was designed to satisfy an extracellular space expansion of approximately 7 per cent of his body weight by the administration of plasma in the first 24 hours, and for this reason he was given 4,800 cc of plasma in the first 24 hours and a total of 18,000 cc of therapy. His urine output during this time was 3,500 cc, an amount indicating that the therapy was excessive. During the patient's second 24 hours, treatment was cut down to 7,300 cc, but the urine output was maintained at 1,700 cc for the 24-hour period, an amount adequate to excrete the normal metabolites. (His non-protein-nitrogen remained normal until his last day.)

Between the second and third days the extracellular space had expanded to 96 per cent above normal, a volume theoretically well in the danger zone of overdilatation (Chart 1)

The patient did not live long enough to mobilize any edema, there was no discernible diuresis. It is possible that his renal function was not adequate to excrete the excess body fluid. Death resulted from a combination of factors including wound infection, excessive extracellular fluid which could not be dissipated by his kidneys, as well as age and debility terminating in bronchopneumonia.

TABLE X  
PLASMA AND EXTRACELLULAR FLUID DATA

Case 268								
Female, Age 83 Weight 60.0 Kg								
Extent of Burn 62 percent total, 22 percent full thickness								
Day	PV		SCNV		Na*V		CL*V	
Post-Burn	cc	% BW	cc	% BW	cc	% BW	cc	% BW
3	2220	3.7	20800	35.0	17670	29.3	10500	17.5

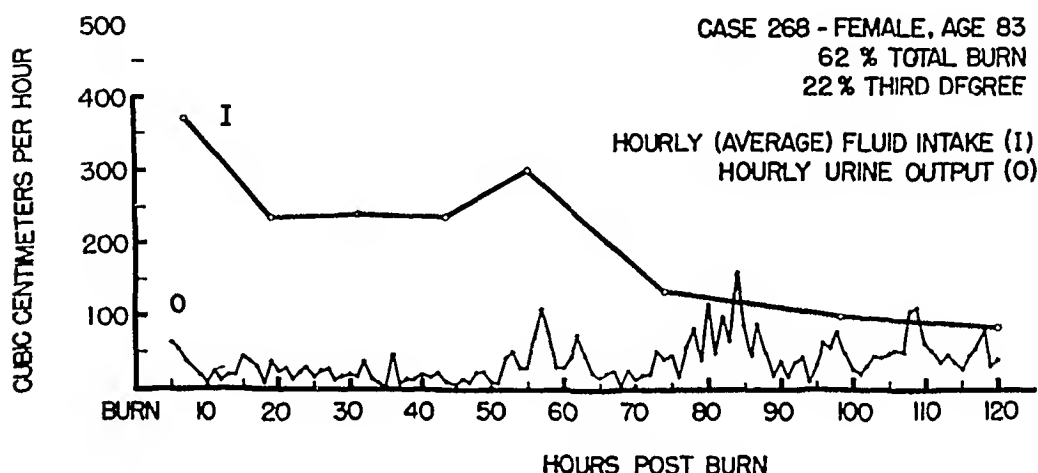


CHART 8—Intake-Output Chart of an Extensively Burned Elderly Woman Treated with Minimal Quantities of Fluids (Case 268)

With the intent of avoiding overhydration, the intake was kept as low as consistent with a minimally adequate urinary output. In the first 72 hours there is a wide discrepancy between intake and output indicating fluid retention. From the 75th to the 86th hour there is a spontaneous diuresis. Despite the patient's age and extent of the burn there was no pulmonary and minimal peripheral edema.

**Case 268**—An 83-year-old female patient was admitted with burns of 62 per cent total, 22 per cent full thickness. Because of her age, fluid therapy, as in Case 234, was given on a limited scale. On the second day she was digitalized. She remained drowsy, became more and more difficult to arouse and uncooperative. Her pulse rate gradually rose and her respiratory rate increased in the last four days reaching a rate of 50. The patient died on the 13th post-burn day with a sudden rise of temperature to 106° and the clinical picture of extensive bronchopneumonia.

Fluid therapy in this patient was carried out according to the scheme that she would require in the first 48 hours plasma amounting to 7 per cent of her body weight (the expected extracellular expansion) plus 1,500 cc of electrolyte-free water to cover insensible losses, and 1,500 cc of electrolyte solution to cover kidney function. Her urine output was to be regarded as adequate if it was maintained between 20 and 50 cc per hour. This regimen was initially successful and although her total urine output during the first

two days of her hospitalization totalled 326 and 515 cc respectively, the patient did not develop azotemia nor did she show evidences of hemoconcentration.

Justification of this course of systemic fluid therapy appeared on her third post-burn day when with an intake of 2,000 cc the urine output was larger than that of any previous 24-hour period and she excreted over a liter of urine daily for five successive days. This spontaneous diuresis indicated that she had been able to mobilize her wound edema. On the day prior to her diuresis, an isolated set of volume measurements was carried out, with the intention of checking her therapy (Table X). Her plasma volume was essentially normal. The thiocyanate space was 75 per cent greater than normal, a volume well in the danger zone of over-distention (Chart 1). The sodium space was approximately 3 liters smaller than that of the thiocyanate. A measurement of her chloride space was carried out for experimental purposes (using radio-chloride) and it proved to be 7 liters smaller than the sodium space.

It never was possible to treat her wounds other than by occlusive dressings, extensive wound sepsis culminated in bronchopneumonia and death at the end of two weeks.

The death of both of these patients was influenced by their advanced age and the extensive, infected wounds. Yet it is striking that both had a distention of their interstitial spaces to the degree found in the younger, excessively treated patient who also died (Case 231).

### External Water Loss

The loss of water externally from the surface of the wound has been determined in seven patients by measuring the quantity of sodium and of chloride in the exudate (Table XI). The loss is roughly proportionate to the extent of the wound surface, is greatest in the first few days, and diminishes with time. As an average for the first 48 hours, 50 cc is lost for each 1 per cent of surface area burned. These direct measurements are more accurate than the indirect calculations made in Table III.

### Appraisal of Surface Area Formula Deductions from Observations Thus Far Made

Analysis of the experience gained from the cases described lead us to a statement of nine conclusions concerning the nature of the fluid disorder of thermal burns and to the recognition of two opportunities to improve on the surface area formula for planning the fluid therapy of the extensively burned patient.

1. A relentless expansion of the interstitial fluid volume takes place in the first 36 to 48 hours following a burn. This expansion in the extensively burned patient exhausts the water and protein resources of the plasma and dehydrates the rest of the body if untreated. Inadequate therapy results in renal and other visceral failure.

2. Fundamentally this increase in interstitial fluid volume is the edematous distention in the area of the wound, and the amount of expansion is therefore proportional to the area burned.

3. The proportion is, however, not direct, for as the area burned increases to 30 per cent of the body surface, the expansion of the interstitial space may have already reached a maximum so that the entire extracellular space is 50



per cent above the normal volume (that is, an extracellular space of 30 per cent of body weight) The amount of edema accumulating as the result of a burn to skin depends to some extent upon the specific area burned (face, scrotum and buttocks, for instance, can accumulate more beneath the skin than arms and legs) and upon relocation of this edema from burned to unburned areas (as

TABLE XI

EXTERNAL WATER LOSS CALCULATED FROM EXUDATE SODIUM AND CHLORIDE LOSSES  
ASSUMING THESE IONS LEAVE THE WOUND AT CONCENTRATIONS FOUND IN EXTRACELLULAR FLUID

Days Post-Burn	Sodium Loss Gm (Total)	Fluid Loss on Basis of Na cc /Day	Chloride Loss Cm	Fluid Loss on Basis of Cl cc /Day
<i>A Circumscribed Partial Thickness Burn</i>				
Case 264 55% Burn of Partial Thickness				
0- 3	2 0	153		
<i>B Extensive Partial Thickness Burn</i>				
Case 254 45% Total Burn, 5% Full Thickness				
0- 4	4 9	375		
5-11	7 8	400		
12-21	5 2	158		
22-31	3 9	119	4 8	131
32-41	4 1	124	3 6	100
42-51	1 5	46	1 2	33
52-61	0	0	0	0
<i>C Extensive Full Thickness Burns</i>				
Case 260 28% Total Burn 12% Full Thickness				
0- 4	4 7	360	3 9	265
5-11	12 1	616	9 8	432
12-21	11 7	356	14 4	390
Case 269 27% Total Burn 20% Full Thickness				
0- 4	15 5	1180	17 3	1175
5-11	14 1	720	14 5	660
12-21	27 9	850	40 8	1110
Case 234, 55% Total Burn 45% Full Thickness				
0- 4	18 5	1400		
5-11	25 3	1100		
Case 268, 62% Total Burn 22% Full Thickness				
0- 4	25 5	1700	30 9	2110
5-11	15 4	1175	18 9	860
Case 262, 85% Total Burn 58% Full Thickness				
0- 4	30 7	2350	20 0	1352
5-11	36 8	1870	24 0	1083

for example by gravitation of head edema to the neck and upper thorax) A more extensive surface area burn is not necessarily accompanied by any further expansion

4 There is a limit to which the extracellular space can expand and the organism survive An expansion of this space more than 50 per cent over

normal is fraught with danger, the mechanism for disposal of the excess fluid may not be adequate when resorption of edema takes place, and an inordinate expansion of the extracellular measurement in itself indicates widespread changes in permeability

5 Over-zealous therapy may exaggerate the extracellular space expansion

6 Renal function is a sensitive index of the balance between tissue thirst, quenching, and over-satiation

7 External loss of fluid is minor compared with the pooling of edema in the area of the wound, yet it is large enough to be taken into account in therapy. The volume can be estimated on the basis of the area of the wound

8 Evidence is lacking that pressure dressings materially limit the fluid requirements of the burned patient. Edema fluid is displaced proximally by such dressings.

9 Resorption of edema has started as a rule by the 45th to 50th hour, it may be rapid and overwhelming if fluid therapy is not promptly curtailed

Although the administration of fluid therapy on the basis of the surface area formula represents a distinct improvement over that based on hemoconcentration, there are shortcomings. The surface area formula does not take into account variation in the volume of edema according to the body area burned and the depth of injury, the relocation of the edema from burned to unburned areas, and the probability that multiple small burns strategically located may overload the lymphatic trunks of one area and lead to a disproportionately large accumulation of fluid. The formula also neglects the complication introduced by damage to the respiratory tract and the factor of size of the patient. Pulmonary damage may increase the requirement for fluid, but it also invites drowning. As for the size of the patient, it is obvious that there is more edema beneath 1 per cent of the skin of a large man than 1 per cent of a small woman or child. But the most important shortcoming of this formula is the absence in it of any idea of restraint. On the contrary, there is in it a temptation to over-estimate the extent of the area burned. Our difficulties have resulted from over-zealous treatment.

Since the interstitial space expansion can be predicted, the needs of the patient can be satisfied by basing therapy on the anticipated expansion, both in volume and in time. Such an approach might make up for the deficiencies of the surface area formula, it should insure adequate therapy in patients with burns of 30 to 50 per cent of the body surface and restrain over-zealous treatment in patients with burns of 60 to 100 per cent. It would tend to limit the amount of fluid which must be excreted once resorption starts. The observations that the three of our patients whose extracellular fluid volume expanded more than 50 per cent over normal died, and that renal function is a sensitive index of the state of hydration, lead to the concept that both the anticipated interstitial space expansion and renal function could be used in planning and guiding therapy.

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\* Dr. D. W. Richards, Jr., has also emphasized the importance of avoiding excessive fluid therapy in the extensively burned patient.<sup>25</sup>

## Formula Based Upon Anticipated Interstitial Space Expansion

The following formula, based on the anticipated interstitial space expansion, is suggested for the fluid therapy during the first 48 hours of the patient burned 30 per cent or more of the body surface

Fluid is to be given to replace that lost in four ways as (1) wound edema, (2) from the wound surface, (3) urine and (4) insensible water. The first two are wound fluid, in composition the same and are logically therefore considered together. The protein concentration of this fluid is approximately 4 per cent, two-thirds that of plasma, while the electrolyte content and concentration equal that of plasma.<sup>4</sup>

In the first 48 hours the following amounts are to be given

1 For wound edema, a volume equal to 10 per cent of the body weight

2 For external loss an amount varying according to the area of wound surface

Burns of 25-35 per cent	= 1,000 cc
35-60 per cent	= 2,000 cc
60 per cent and over	= 3,000 cc

Add 1 and 2, two-thirds of this combined volume is given as plasma and one-third as non-colloid isotonic electrolyte solution. This 48-hour ration is divided into four equal parts, two parts are scheduled for the first 12 hours, one part for the second 12, and the fourth part for the second 24-hour period. This rationing, weighted in the first 12 hours, takes into account the fact that the redistribution of fluid occurs most rapidly in the initial hours after injury. The time intervals are, of course, calculated from the time of burn and, if the patient enters six hours from the time of burn, the subsequent six hours must include the administration of the full 12 hours' ration.\*\*

3 For renal excretion, 1,500 cc for each 24 hours, 3,000 cc total, of non-colloid fluid. One-half is to be given as isotonic electrolyte intravenously. The other half as glucose in water if given intravenously or as palatable fluids if by mouth.

4 For insensible loss, 1,500 cc for each 24 hours, 3,000 cc total, of non-colloid, non-electrolyte solution, glucose in water if given intravenously, or palatable low salt fluids if by mouth.

It would be unreasonable to expect this formula alone to suffice for clinical care because hourly alterations in rate of water-transfer and excretion occur, insensible and surface losses are at best estimates and the water resulting from

\* The protein concentration of the wound fluid is described in the following paper<sup>27</sup>

\*\* For example, in a 70 kg man with 50 per cent of his body surface burned the volumes for the first 48 hours would be as follows

10 per cent body weight	= 7,000 cc
External loss	= 2,000 cc

Total	9,000 cc
Two-thirds as plasma	= 6,000 cc plasma
One-third as saline	= 3,000 cc saline

This 9,000 cc is to be given in the time schedule outlined in the text

metabolism is variable. As with the surface area formula, there is need for a sensitive and significant means of following the clinical progress of the patient.

### Renal Output as Adjunct to Plan of Therapy

As experience accumulated it became evident that our previous methods of evaluating the day to day or hour to hour course of a burned patient were not wholly satisfactory. Hematocrit provided a measure of inadequate plasma therapy, if it remained consistently over 55, shock and oliguria resulted. Between this and the production of hemodilution and edema by over-administration of fluid there remained a wide area in which hematocrit, plasma protein concentration and body space measurements were poor guides. If one administered treatment until the hematocrit fell into the thirties, it was already too late to remedy the serious waterlogging evidenced by the hemodilution.

The simplest index of the state of balance between needs and therapy that we could discover was an hour to hour vigil over renal output. This was provided by placing an indwelling catheter in the bladder, letting it drain by gravity into a small vessel, and recording hourly the amount and specific gravity of the urine. The value of this maneuver in Case 149 has already been described in detail. Charts based on the average intake and output of other cases whose problems have already been discussed are shown in Charts 3 through 8. These quantitative urine output data in general indicate three types of situations commonly encountered in which the usefulness of this method was most readily apparent.

Adequate hourly outputs in the normal to high range (50 cc or more per hour up to 200 cc per hour) bespeak the adequacy of therapy and warn against increasing fluid intake.

A falling or low hourly output (30 cc per hour down to 5 cc per hour for three hours or more) calls for immediate increase of therapy, a necessity not evident for many hours if the hematocrit alone is used. The earlier the low urine output appears after the burn, the more pressing the need for increased therapy.

Hourly urine outputs over 200 cc per hour for more than six hours signify over-treatment if encountered in the first 48 hours or spontaneous diuresis if after the 48th hour. This hourly volume calls for a drastic cut in fluid administration if one is to avoid plethora, pulmonary edema or congestive heart failure.

There was one finding, however, which was equivocal, using the hourly urine output as an index of therapy. This was a continued low output (0 to 30 cc per hour) for many hours in the face of continuing therapy. Under these circumstances two opposite explanations offer themselves, and it is of the greatest importance to distinguish between them.

1. The therapy underway may be inadequate, or
2. A renal lesion is present (due to anoxia,<sup>26, 29</sup> dehydration, hemoglobinuria<sup>30, 31, 32</sup> or damage antedating the burn) which renders more output impossible, and in the face of which any increase in therapy is even more apt to produce edema and heart failure.

The differentiation of these two fundamentally different causes for the oliguria can be accomplished by administering 1,000 to 1,500 cc of fluid rapidly by vein (40 to 60 minutes), a procedure termed the water tolerance test. This amount of infusion has not been deleterious in our experience if not continued over 60 minutes. It may constitute but a small fraction of the day's intravenous ration. The renal response is most significant. If a clear-cut increase in hourly urine output occurs, one may conclude that the kidney is able to handle the water but that the wound demand is not being met by the previous course of treatment. On the other hand, if there is no renal response, one should exercise considerable caution in continuing intravenous therapy on an extensive scale.

The exact nature of the fluid administered for the water tolerance test depends to some extent on the situation in which the patient is found. In most of the instances in which this type of infusion has been used to test kidney function we have used a 5 per cent solution of dextrose in distilled water. In one or two patients in whom salt had purposely been restricted because of age or preexistent cardiac disease, the possibility existed that oliguria represented a salt deficit as much as a water deficit and for this reason the water tolerance test infusion has consisted of normal saline. In one patient (Case 149) therapy was over-weighted with non-colloid-containing solutions at the time that the oliguria occurred and he also showed severe hemoconcentration with respect to red cells, it was clear that the test infusion should consist of plasma.

In any case the infusion is run in so rapidly that a transient plasma volume change is produced regardless of the infusing material. The use of plasma for such a water tolerance test should be approached with caution because, in the absence of a plasma deficit, cardiac embarrassment may be produced, even in the absence of overt myocardial disease.

### **Trial of the Volume Expansion Formula and Renal Function Guide**

Since the fluid therapy of burned patients is a problem only in the extensively burned, trial of the new plan of therapy, based on the anticipated increase in volume of the interstitial space and refined by attention to the renal function, was made upon patients with such burns. Five cases have been selected with full thickness burns who were so treated and in whom adequate measurements of water balance were made to permit comparison of the method with that of the surface area formula. There were two fatalities, both patients had respiratory tract injury. Only one patient had early excision and grafting of the full thickness wounds. Since the importance of these cases lies in the details of their care and response, they are presented separately.

**Case 260 (Chart 9)**—A 27-year-old tuberculous woman received burns of 28 per cent total, 12 per cent full thickness. The burns were distributed around the trunk and arms with some areas on lower abdomen, buttocks and legs. After the initial phase of fluid imbalance had been controlled, on the 9th post-burn day the critical areas in axilla and popliteal space were excised and grafted. Healing elsewhere was gradual and she was discharged on the 94th day.

By plan she was to have received 5,500 cc of plasma, 5,500 cc of saline for wound

dilution and external loss (an overestimate of saline), 2,000 cc of saline for urine output, and 3,000 cc of dextrose in water to cover lung losses in her first 48 hours. This scheme was not adhered to, as her plasma totalled only 3,650 cc in the first 48 hours (plus one whole blood transfusion). Her saline, at 7,100 cc, was essentially that outlined. The water (electrolyte-free) intake totalled 5,600 cc. During the first 48 hours she lost 1,545 cc as vomitus and could take nothing effectively by mouth.

By 10 to 12 hours after injury, her urine output had dropped to 0 to 25 cc per hour and her intravenous intake was therefore accelerated, and for two hours she received a rapid infusion (approximately 1,000 cc per hour) of 5 per cent glucose in water (Chart 9). This was followed by a rise in urine output to 400 cc per hour indicating that her previous rate of infusion was too slow. Her maximum hematocrit of 52 per cent just previous to the water tolerance test dropped to 44 per cent the next day.

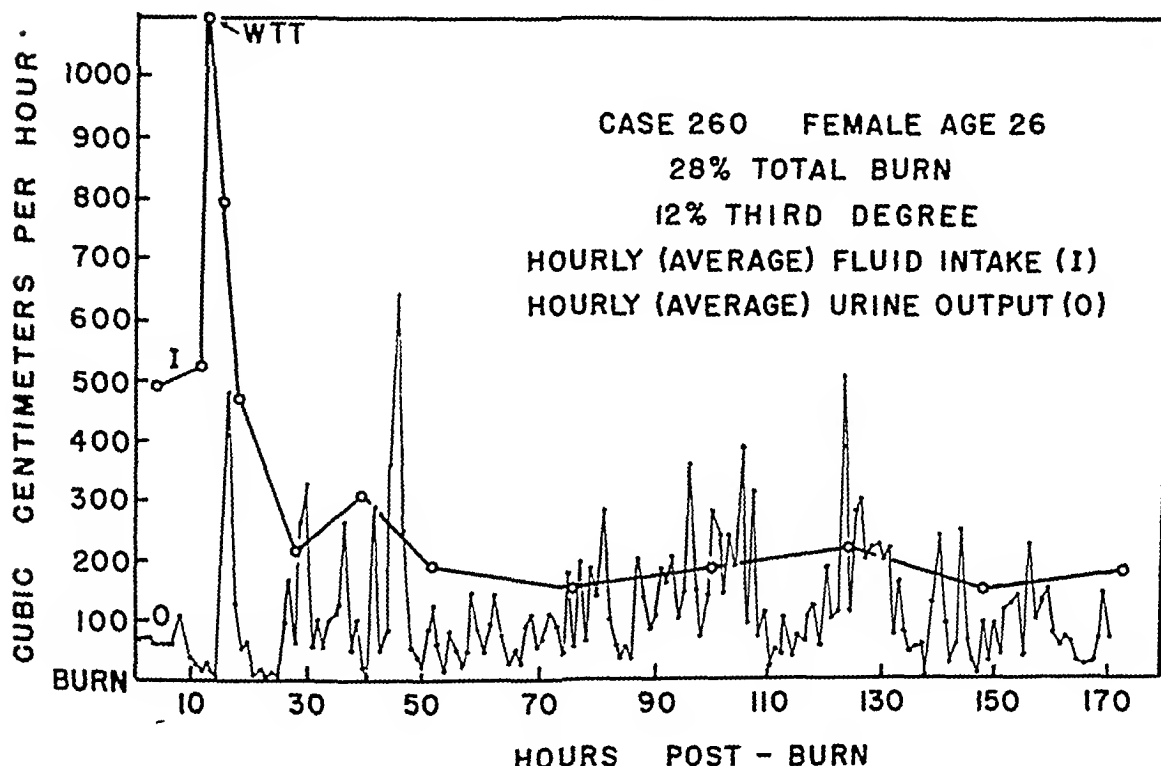


CHART 9—Intake-Output Chart of a Patient with a Total Burn of 28 Per Cent Demonstrating the Use of the Water Tolerance Test (Case 260)

Therapy was begun and a customary intake-output discrepancy was observed as one would expect in a burn of this magnitude. At the 10th to 14th hour, urine flow practically ceased. Therefore, a rapid infusion was begun and there was a gratifying response in urine output, indicating that the needs of the wound were not quite being satisfied by the earlier therapy. As soon as this rapid infusion was stopped, however, urine flow again fell to a low level and therapy should have been increased. At 30 hours the patient responded with a spontaneous diuresis, indicating that the peak of edema formation was approaching and that the period of oliguria had not been long enough to produce renal damage. Had the two periods of low renal output occurred several hours earlier, when the rate of edema formation presumably was at its height, the failure to increase the rate of fluid therapy following the water tolerance test might have been followed by renal damage.

Case 262 (Chart 10)—A 64-year-old Portuguese male admitted 10 hours after sustaining burns covering 85 per cent of his body surface. Fifty-eight per cent was of full thickness destruction, some of it deeply charred. His course was steadily downhill after the fourth post-burn day, he coughed up blood-tinged sputum and died of respiratory failure with respirations up to 70 per minute on his 8th post-burn day. Postmortem examination showed generalized arteriosclerosis, an hemorrhagic pulmonary lesion, nephrosis and nephrosclerosis.

On admission the patient showed hemoconcentration with an hematocrit of 65 per cent and plasma protein of 7.7 Gm/100 cc. His estimated body weight was 60 kg. Because of the 10-hour lapse and presence of established shock the fluid ration was heavily concentrated in his first 12-hour period.

The expansion formula was followed and in his first 12 hours he received 4,250 cc of plasma, 5,000 cc of other intravenous fluids (3,000 of which were saline) and one whole blood transfusion. His response to this was gratifying. He rallied clinically, his urine output rose from near zero levels to 100 cc per hour and in the next 12 hours to 200 cc per hour (Chart 10). His hematocrit fell to 40.2 per cent and his non-protein-nitrogen to 48 mg/100 cc (from a level of 55 mg/100 cc on admission). By his 40th hour, urine output was sufficient to justify lowering his intake to less than 200 cc per hour and despite this he maintained good urine output, indicating a tendency to diurese his edema.

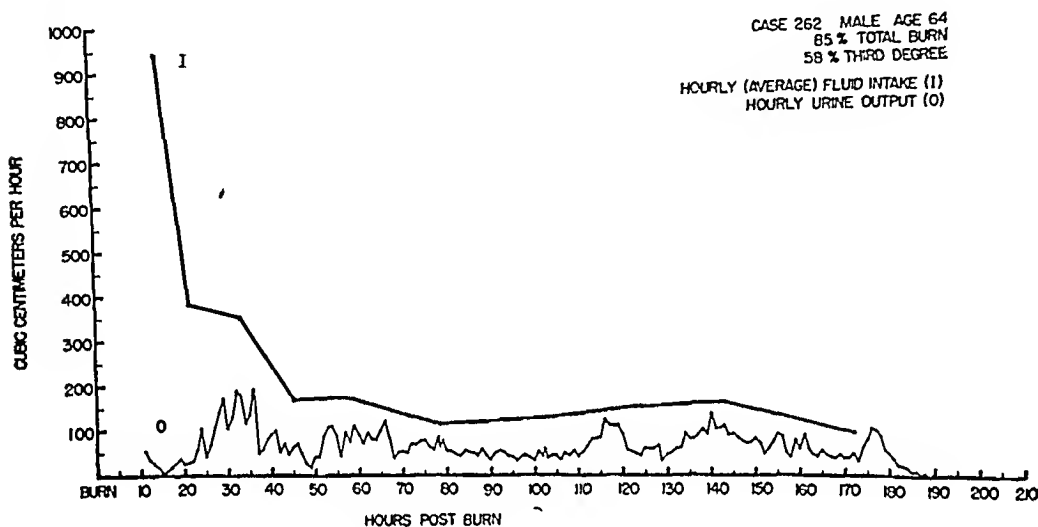


CHART 10—Intake-Output Chart of an Elderly Man with a Burn of 85 Per Cent Who Succumbed (Case 262)

An early high intake-output discrepancy indicates the amount of fluid required to satisfy the demands of the wound in this patient before a satisfactory urinary output appeared at the 23rd hour. Thereafter, intake was cut down to a level adequate to maintain normal urine flow until 185 hours post-burn at which point the patient became oliguric despite therapy and died. Postmortem examination showed preexisting renal disease in addition to extensive wounds.

From this point on, however, he failed to improve, his non-protein-nitrogen remained elevated and terminally, with a temperature of 104, pulse rate of 160 and respiration rate of 70, anuria developed, preceding death by three or four hours. The terminal events were those of respiratory tract burn, evidenced on admission by burn of the nares and pharynx and leading to cyanosis, pulmonary exudate and death.

**Case 269 (Chart 2)**—A 60-year-old luetic alcoholic was admitted 22 hours after receiving burns totalling 27 per cent with 20 per cent full thickness. On admission the patient was in borderline circulatory failure with an hematocrit of 59 per cent which, during the first 12 hours of therapy, fell to 52 per cent, and then dropped to the range of 38 to 42 per cent where it remained for a week.

Because of the 22-hour lapse before therapy, and despite the elevated hematocrit, he was given a whole blood transfusion initially. By plan he was to receive 3,000 cc of plasma in his first 12 hours in the hospital, with lessening amounts thereafter. It was hoped that a water intake of 2,500 cc could be attained orally in his first 12 hours. If not, suitable intravenous supplement was planned. This plan was adhered to and he received

4,200 cc of plasma in his first 32 hours in the hospital in a total treatment regime of 16,000 cc of which 5,300 cc were orally administered

Urine flow almost ceased from the 27th to the 32nd hours (Chart 2) A water tolerance test was given which was followed by a diuresis lasting for nearly 12 hours This diuresis indicated that the earlier therapy had been more nearly adequate than suggested by the low urinary output

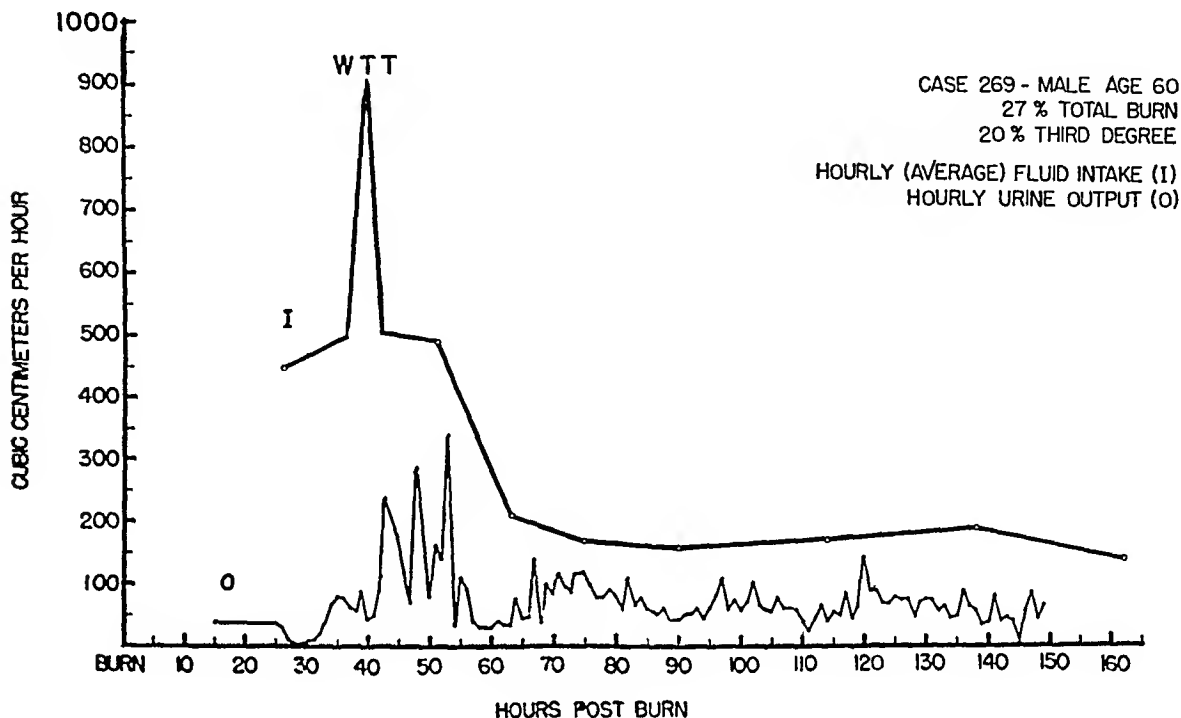


CHART 11—Intake-Output Chart in a Patient with a Moderately Severe Burn Demonstrating a Response to the Water Tolerance Test at 40 Hours, Administered Because of Low Output Rates in the Previous Eight Hours (Case 269)

An obvious diuresis was produced which lasted almost 12 hours, indicating that the demands of the wound had previously been met more satisfactorily than revealed by the earlier transient low urinary output

Case 280—A 40-year-old feeble-minded male was brought to the hospital within three hours after receiving burns of a total of 58 per cent, 45 per cent estimated as full thickness There were obvious burns of nose, pharynx and larynx Seven hours after entry a tracheotomy was done He died seven days after entry with evidences of pulmonary tract burn as the chief cause of death Three days before death, laryngoscopy showed necrosis of hypopharynx, epiglottis, esophageal orifice and larynx as far down as could be seen

The plan called for 20,000 cc in 48 hours, half of this in the first 12 hours This plan was not strictly adhered to because of an adequate renal output with slightly lesser amounts of therapy, and in the first 18 hours he received but 3,000 cc of the 5,000 cc of plasma planned (This demonstrates the flexibility of the hourly urine output technic and the ease with which a decrease in ration may be adjudged safe) His kidneys put out 25 to 180 cc per hour, averaging 100 cc per hour during this time Because of this, a diminution in ration was adopted and despite his airway burn, the patient did not develop pulmonary edema and maintained an excellent tracheotomy airway and tidal volume until 24 hours before death, when obstruction due to necrosis in the trachea developed

Case 281 (Chart 12)—A 26-year-old woman entered the hospital because of burns of 32 per cent total, 25 per cent full thickness The right arm was so deeply burned that on



the 8th day amputation at the mid-forearm became necessary with excision of the burns of the remainder of the arm. The grafts took satisfactorily, but 13 days after the initial amputation, reamputation through the mid-humerus was necessary because of sepsis in the elbow joint. From then on the patient's course was uneventful.

The plan of treatment included 5,000 cc of plasma, 3,000 cc of saline and 2,000 cc of glucose in water for the first 48 hours. This regimen was followed, but the morning following the burn the hourly urine output was continuing low (10 to 15 cc per hour for 3 hours) and, therefore, a water tolerance test was performed (Chart 12). A response

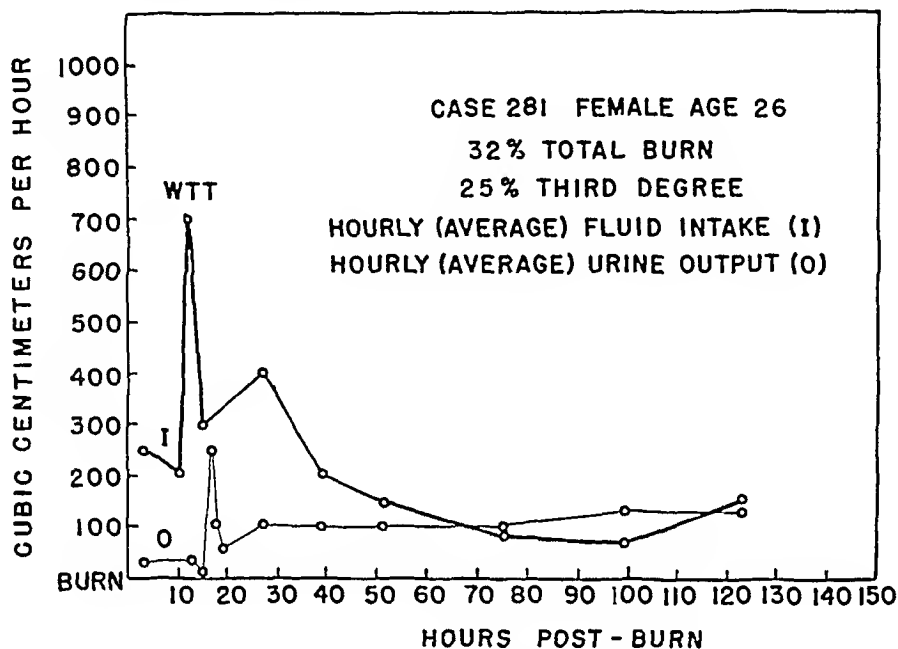


CHART 12—Intake-Output Chart in a Patient with a Deep Burn of the Upper Extremities Requiring Amputation (Case 281)

Response to a water tolerance test given at the 12th hour post-burn indicated the need for more intensive therapy, which was accordingly given. At the 40th hour the intake and output relation was normal. From the 70th to the 115th hours, the output exceeded the intake pointing to resorption of wound edema.

with an output of 250 cc for the first hour, then 110 and 90 cc showed that kidneys could function satisfactorily if provided with enough fluid, the intravenous ration was increased, renal function remained optimal from then until healing.

The patient had a spontaneous diuresis on the second post-burn day when, with a sharp fall in intake, the urine output was maintained and then gradually rose. This diuresis was presumably occasioned by beginning resorption of wound edema.

#### SELECTION OF FLUID FORMULA

By what formula shall the fluid therapy of the extensively burned patient be guided in the first days after injury? For normal-sized adult patients, burned up to 50-60 per cent of their body surface, the surface area formula, guided by the renal output, is a safe and sufficient method of planning the fluid therapy for the first 48 hours, for more extensive burns or in patients of unusually large or small habitus, the formula may be misleading. In patients whose burn is 30 per cent or more, the expansion of the interstitial portion of

the extracellular space may become maximal, and the formula based on expected extracellular space expansion will also apply satisfactorily. It, too, should always be used in conjunction with the renal output guide. Whichever formula is used, one must not hesitate to depart from plans and admit errors in prediction if the kidneys protest.

After 48 hours, with either formula, a regimen similar to the second 24 hours is maintained until the kidneys indicate the onset of diuresis and fluid therapy is immediately curtailed. At this point a shift over to controlled and restrained oral intake may often be made. In patients with burns predominantly of partial thickness, the diuresis appears promptly and may be massive since resorption of edema may proceed at a pace almost the equal of formation. In patients with burns of full thickness destruction the resorption of edema is slower and the diuresis therefore less pronounced. The hourly urine figures are usually no longer useful after the 8th day though in occasional cases there may be disquieting periods of oliguria up to 14 days and the urine chart should then be maintained.

During this early period there are many other important considerations such as caloric and vitamin intake, nitrogen intake, red cell replacement, sedation, tracheotomy, chemotherapy, etc.<sup>\*</sup> The outlines of therapy cover only fluid therapy, the other features are dealt with elsewhere.

#### SUMMARY

The extracellular space has been measured in a series of burned patients, patients with other diseases and normal human beings, dehydrated and given therapy. The measurements have included the plasma, thiocyanate and radiosodium volumes.

Almost identical in normal individuals, the radiosodium and thiocyanate volumes may differ in burned patients. In the first days after injury, the radiosodium may be the larger. In the later days, concomitant with wound infection, the thiocyanate volume surpasses that of the radiosodium. These discrepancies point to differential cell permeabilities for the two ions.

In the burned patient an expansion of the extravascular extracellular space or interstitial space is the important feature of the disordered fluid balance, though there is external fluid loss from the wound, the interstitial space is, nonetheless, the chief recipient of plasma loss. Pressure dressings do not effectively limit the interstitial space expansion.

Therapy must be planned to satisfy, and not augment, this pool of wound edema. Over-treatment will exaggerate the defect and in the extensively burned patient will endanger survival.

Measurement of the hourly urine output is the most ready means of checking the adequacy or noting the excess of treatment.

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\* The necessity of special nursing and a professional visit at intervals of only a few hours is obvious from the nature of the measures taken to insure success. The care of an acute burn can, from the point of view of professional care needed, best be compared to diabetic coma or advanced tetanus.

A simple water tolerance test is described which allows a more accurate interpretation of small hourly urine outputs

All of the fluid needed to prevent circulatory failure and dehydration of the body in the first 36 to 48 hours must eventually be excreted by the kidneys or exhaled by the lungs, if not lost in the exudate. When resorption of edema is manifest after the 48th hour, fluid therapy must be promptly curtailed to avoid pulmonary edema. In burns of partial thickness the resorption may proceed almost as rapidly as the formation while in those of full thickness destruction the resorption is generally slower.

The practical application of this knowledge to extensive burns is described. Plans of therapy, based upon the anticipated expansion of the interstitial space as well as the surface area burned, are outlined for patients having a burn of 15 per cent or more of the body surface.

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